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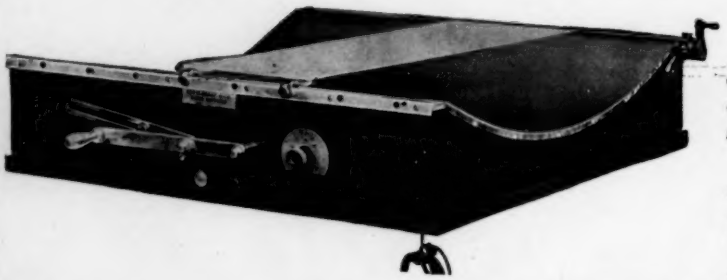

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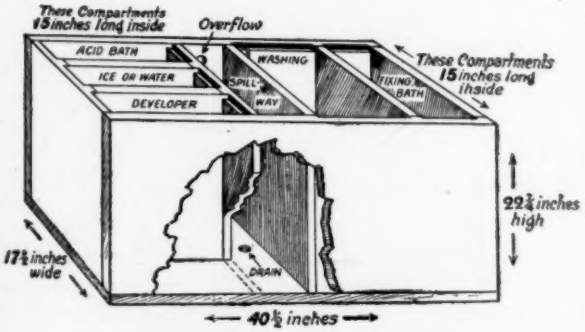

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. X DECEMBER, 1923 No. 12

IONIZATION METHODS OF MEASURING X-RAY DOSAGE*

BY WILLIAM DUANE, PH.D., SC.D.

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BOSTON, MASS

IN this paper and those to which it refers are described methods of measuring *x*-ray dosage by means of ionization currents. The methods have the advantage of measuring, not the power or current put into the tube, plus the voltage, filtration, focal distance, etc., but something associated with the actual beam of *x*-rays employed. They measure what may be defined to be the intensity and the effective wave-length of the *x*-ray beam in terms of certain absolute units, so that the measurements may be compared with similar ones made in other laboratories and clinics.

The methods have a further advantage in that the deflection of the instrument as read on a scale gives the value at each instant of time of the intensity of the *x*-radiation at the place where the detecting instrument lies. It is thus possible to determine at any time during a treatment the intensity of the *x*-radiation entering the patient's skin or emerging again on the other side of the body. Further, the instrument may be used to determine the percentage of radiation coming through a filter of any substance or thickness, the amount of scattered radiation coming from a patient or from the filter in different positions, etc., etc.

The paper contains a few illustrations of the many possible applications of these methods. A series of experiments are described illustrating the measurement of depth doses in water-phantoms. Measurements of the intensity of the *x*-ray beam at points at different distances from the surface of the phantoms along the axis of the beam will be given. By means of the isodose charts, the intensity at any point in the phantom can be determined. Such charts should be mapped out for each particular kind of *x*-ray plant employed, and also with varying volumes of water, so as to reproduce as nearly as possible the conditions obtaining in the actual treatments of patients. The measuring instrument described below enables one to do this with reasonable precision. As these charts give only a rough estimate of the intensity of the radiation itself, at points in the body of a patient, and as so many of them have already been published in recent literature, it does not seem necessary to reproduce similar ones here.

The paper concludes with a brief account of some experiments carried on in our own laboratory on the wave-lengths (and therefore the penetrating powers) of *x*-rays scattered by various substances. The problem of scattered radiation has become one of great importance, not only from the point of view of the patient but also from that of the operator himself. Our careful measurements with an accurate *x*-ray spectrometer have revealed the fact that scattered radiation contains a large number of rays that are just as short, and therefore just as penetrating, as the primary rays.

* The author of this paper was awarded first prize, $500.00, in the Leonard Prize contest.

The ionization effect of *x*-rays forms the basis of the methods of measurement described in this paper.

In February, 1896, Sir Joseph Thompson announced the discovery of the fact that the *x*-rays observed the year before by Roentgen, when they pass through a gas, make of it a conductor of electricity. Benoist and Harmozescu in France and Righi in Italy observed the same phenomenon at about the same time. According to the researches made since the discovery of this phenomenon, the *x*-rays split up molecules of the gas into charged particles,

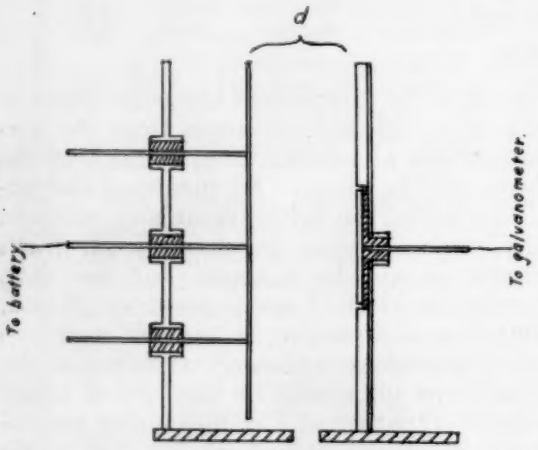

FIG. 1. Standard ionization chamber with variable distance between plates.

some of which carry positive, and others negative charges. The motion of these charged particles or ions, as they are called, through the other molecules of the gas, carries the electricity through it and thus produces the conductivity. From the name of the charged particles—ions—we call this phenomenon the ionization of a gas.

In modern physics we usually define the intensity of a beam of rays to be the amount of energy carried per second through a square centimeter of a surface imagined to be drawn across the rays perpendicular to them. In the case of *x*-rays we can measure the amount of energy carried by absorbing the rays and estimating the rise in temperature of the material that absorbs them. In order to do this, however, we require exceedingly delicate apparatus and great skill in experimentation. A method of estimating the intensity of *x*-rays by means of their heating effect does not seem, therefore, to be a practical method of estimating dosage for every-day use, and we are forced to employ, as a means of determining their intensity, some other effect produced by the rays. At present, the ionization effect appears by far the best. It may not be out of place to mention that an ionization current depends upon the amount of radiant energy *absorbed* by the gas. This is an advantage, for it is the energy absorbed by the tissues that produces the effect in therapy.

The ionization methods of measuring *x*-ray dosage here referred to have already been described at some length in THE AMERICAN JOURNAL OF ROENTGENOLOGY (Dec., 1922, p. 781, and May, 1923, p. 399). We will, therefore, refer the reader to these previous publications for details.

In using a standard ionization chamber to calibrate other chambers, care must be taken to include practically all the ionization effects of the *x*-rays.

In order to determine experimentally how far apart the plates must be in order to include practically the whole amount of ionization produced by the *x*-ray beam, I designed the standard ionization chamber represented in Figure 1. The plate attached to the battery is movable and can be shifted so as to vary the distance, *d*, between it and the plate joined to the galvanometer. The lead end of the ionization chamber was not attached to the rest of the instrument so that the hole in it could be shifted in such a way as to allow the beam of *x*-rays to pass always halfway between the plates.

The following table contains the deflections of the galvanometer with the plates placed at different distances apart when this ionization chamber was used in the electrical circuit.

Distances between plates *d* (cm.)	Deflection of galvanometer (mm.)
2.2	28.2
3	29.2
4	30.6
5	30.8
6	30.4
7	30.6

In this experiment the constant voltage applied to the tube amounted to about

200,000 volts and the effective wave-length was .15 Ångström.

It appears from the data contained in the table that no increase in ionization current occurs if the distance between the plates is increased beyond about 4 cm. Hence a distance of 4 or 5 cm. between the plates suffices to include the effects of substantially all of the secondary radiation within the limit of error of the measurements.

In order to measure currents a galvanometer must be calibrated. The calibration consists in sending a known current through the instrument and reading its deflection. The best method of obtaining a known small current such as those employed in *x*-ray dosage measurements is to use a standard cell joined to standard resistances. The standard cell and resistances are fastened in a box and the circuits joined electrically to the galvanometer. A plug contact in the box enables one to send the standard current through the instrument at any desired time. It is convenient to have the standard resistances so chosen as to send a current through the galvanometer equal to that which would be produced in the ionization chamber one is using, if the ionization chamber lay in an *x*-ray beam of one-tenth of a unit. With such an arrangement of circuits all that is necessary in order to measure the intensity of the *x*-ray beam in absolute units is to read the deflection due to the ionization chamber and also that due to the standard cell. Then divide the former by the latter and multiply the quotient by one-tenth. The result is the intensity of the *x*-ray beam in the absolute electrostatic units. These I have called E units.

It is perhaps superfluous to call attention to the fact that in estimating dosage—erythema dose, for instance—it is necessary to measure the effective wave-length of the beam as well as its intensity, for the amount of *x*-ray energy absorbed by the tissues depends upon the wave-length.

These wave-length measurements may be made with either a standard ionization chamber or one of the smaller chambers. It is sometimes advisable to standardize the smaller chamber for wave-length measurements as well as for intensity measurements, by comparison with the standard ionization chamber. If, however, the plates in the chamber are carbon, the wave-length calibration does not appear to be necessary.

The methods of estimating the *effective* wave-length of an *x*-ray beam I described in THE AMERICAN JOURNAL OF ROENTGENOLOGY for March, 1922, on pages 170 and 171, and also for December, 1922, on pages 788 and 789. It consists in measuring (by means of an ionization chamber, for instance) the fraction of *x*-radiation that passes through a sheet of copper of given thickness. From this fraction the effective wave-length may be read off by means of a curve which represents the fractions of *x*-rays of different wave-lengths that pass through the plate, the wave-lengths having been measured by means of an *x*-ray spectrometer. For details of the methods the reader is referred to the above-mentioned papers.

One important feature of this method lies in the fact that the reading of the galvanometer gives, not the total dose received by the patient, but the intensity of the *x*-ray beam at a given instant of time. In order to get the total dose we must multiply the intensity by the time of exposure.

It is important to determine and record both the intensity factor and the time factor of *x*-ray doses; for many effects produced by the rays are not proportional simply to the product of the two factors. It seems likely from some recent estimates of erythema dose made by means of these ionization chambers that the erythema produced in the skin by *x*-rays is not always proportional to the product of the intensity by the time of exposure. Some of our recent estimates of erythema indicate that if one reduces the intensity to one-half its value the time required to produce an erythema must be more than double.

The large, standard ionization chambers are not suitable for measurements of the intensity of the *x*-rays received by the patient during a treatment. We invariably use one of the small ionization chambers for this purpose. We measure the intensity of the rays at the surface where they enter the patient's body, and also

where they emerge. This gives us an estimate of the secondary radiation coming from the patient's body. The estimate, however, is too low. Estimates may be made by means of water-phantoms, placing the small ionization chamber in the water itself. This estimate is always too high. The real dose received by the patient's skin lies between the two. We have obtained quite variable estimates of the secondary radiation from different patients made by measurements taken during the treatments themselves. The secondary radiation appears to depend not only upon the size of the portal of entry, but also upon the size of the patient and the shape, content, etc., of the portion of the body radiated. In estimating erythema doses all these factors must be taken into consideration. The safest method is to make the measurements while the patient is actually being treated.

In many of the ionization methods of measuring dosage one determines the ionization current by timing with a stop watch the passage of the leaf of an electroscope across a scale. In methods of this kind some difficulty often arises in determining whether the current is saturated or not. Very particular attention should be paid to this point. Other sources of error in such measurements are mentioned on pages 404 and 405 of THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, for May, 1923.

As illustrations of this method, let us consider the following problems: Firstly, to measure the intensity and effective wave-length of an *x*-ray beam by means of one of the standard ionization chambers. The apparatus having been set up, the closing of the standard cell circuit produced a deflection of 24.5 mm. The ionization current due to the *x*-ray beam passing through the standard ionization chamber produced an average deflection of 16.1 mm. On adding a sheet of copper having an average thickness of .50 mm. the deflection due to the *x*-rays passing through the standard ionization chamber fell to 10.4 mm. The standard cell produced a current of 5 e.s.u. through the galvanometer. The volume of air in the standard ionization chamber from which the ions came to the plate connected with the galvanometer was 25 cm. Hence, an *x*-ray beam producing the same deflection as that due to the standard cell current would have an intensity of 5 divided by 25, in other words, of 0.2E. To get the actual intensity of the *x*-ray beam we therefore divide 16.1 by 24.5 and multiply the quotient by 0.2. This gives 0.131E as the intensity of the *x*-ray beam expressed in these absolute electrostatic units, the E units.

To get the effective wave-length we divide the deflection after ½ mm. of copper has been added to the filter, namely, 10.4, by the deflection before it was added, namely, 16.1. This gives 0.645. In other words, the radiation coming through the one-half mm. of copper amounts to 64.5 per cent. Referring to the curve representing the fractions of the radiation of different wave-lengths getting through the one-half mm. of copper, we find that the effective wave-length is about 0.164.

The intensity and effective wave-length of an *x*-ray beam depend to a considerable extent upon the type of generator employed and the way in which it happens to be running, even though the voltage, as estimated by a sphere-gap, the current through the tube, the filtration and distance from the tube, may be given. It is impossible, therefore, to state accurately what the intensity and effective wave-length of a beam may be under the above-given conditions. Actual measurements have shown, however, that the intensities of *x*-ray beams 50 cm. from the tube after they have passed through 2 or 3 mm. of aluminum and with voltages of 80,000 to 100,000 volts, and currents through the tubes of 3 to 5 ma. range in the region of intensities between 0.1 and 0.5 e.s.u.

The *x*-rays from a tube running at a voltage in the neighborhood of 200,000 volts with 3 or 4 ma. passing through the tube and with a filter of ½ to 1 mm. of copper, have intensities ranging from 0.1 to 0.2 at a distance of 50 cm. from the target. Certain types of commercial machines, however, produce similar intensities only when running at 230,000 to 240,000 volts.

The effective wave-lengths of the *x*-rays after they have passed through 2 or 3 mm. of aluminum lie between 0.4 and 0.5°

Ångströms, if the voltage applied to the tube lies between 30,000 and 40,000 volts. For voltages between 80,000 and 100,000, and with filtration of 3 to 4 mm. aluminum, the effective wave-lengths lie between 0.2 and 0.3° Ångströms. If the voltage be raised to 200,000 volts or thereabouts, the *x*-rays coming through a filter of ½ to 1 mm. of copper have wave-lengths lying in the range from 0.14 to 0.17 Ångströms. These wave-lengths are somewhat shorter than those of the characteristic *x*-rays of the tungsten target (namely, .184, .209 and .213). Their exact positions with reference to the tungsten line spectrum may be seen by referring to the above-mentioned articles in THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY.

The effective (or average) wave-length should not be confused with the shortest wave-length in the spectrum, which is always given by the relation $V\lambda = 12{,}350$, where V represents the maximum voltage applied to the tube.[1]

In order to calibrate one of the small ionization chambers by means of a standard ionization chamber, we need only to measure the same beams of *x*-rays with each of them. The ratio of the galvanometer's deflection with the small chamber to that with the standard chamber gives us a certain factor, which, if the chambers are properly constructed, is substantially the same over a certain range of wave-lengths. This range may be considerably increased by using graphited paper as electrodes in the chamber. We may employ the factor in calculating the intensities of the *x*-ray beams. A more convenient method, however, consists in changing the resistances in the standard cell box so as to increase the current it sends through the galvanometer in the same ratio. The quotient found by dividing the deflection due to the ionization current by that due to the standard cell may then be used in exactly the same way as in the case of the standard ionization chamber.

As an illustration of one of the uses to which these ionization chambers may be put, let us consider the problem of determining the depth dose of *x*-rays passing through a water phantom.

[1] DUANE and HUNT. *Phys. Rev.*, Aug., 1915, p. 166.

When the ionization chamber lies in the water a great deal of radiation passing through it comes as scattered or secondary radiation from the water surrounding it. The secondary radiation passes through the chamber in all directions, and in order to record the effects due to this secondary radiation it is desirable to have an ionization chamber such that similar rays passing through it in different directions produce at least approximately the same ionization current.

An ionization chamber similar to that represented in Figure 2, D, has been designed for depth-dose measurements in water-phantoms.[1] It consists of a thin,

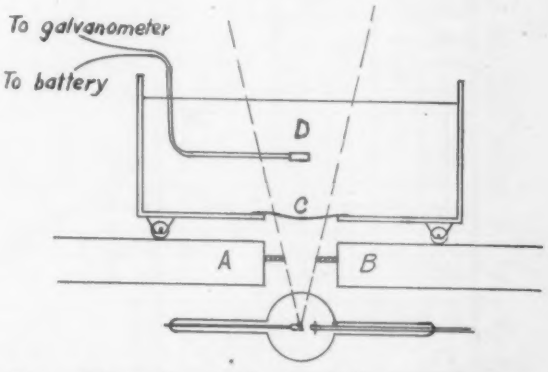

FIG. 2. Water-phantom for depth-dose measurements.

hard rubber box, sealed up tight and covered with a thin rubber bag, so that the water cannot penetrate it. The electrodes consist of thin plates and may be of aluminum or of paper covered with pencil marks. A wire passing through and insulated from a small lead tube connects two of the plates to a battery, and another wire, similarly insulated and protected, connects the third, central plate to a galvanometer. The insulation and lead shielding of these connecting wires are made quite small so as not to absorb any more than necessary of the radiation that would pass through the ionization chamber coming from the water in their neighborhood.

Special experiments have shown that for an ionization chamber constructed in this way the current due to rays passing through it in various directions does not lie more than 4 per cent, on the average,

[1] AM. J. ROENTGENOL. & RAD. TH., May, 1923, p. 399.

below that due to rays passing straight through it.

Figure 2 represents the water-phantom used for this experiment. It consists of a wooden box (30 × 14 × 14 in.) on rollers, that can be moved over the opening in the floor, AB, through which the *x*-rays come from a tube in the room below. A sheet of rubber, C, 2 mm. thick, covers the opening in the bottom of the box. The water in the box causes this rubber covering to sag slightly and to take more or less the form of the human body. The rubber may be taken to represent the skin of a patient.

The calibration of this ionization chamber indicated that if the deflection obtained was the same as that due to the standard cell which produced a current of 5 electrostatic units, the intensity of the radiation passing through the chamber would be $\frac{1}{10}$th of an electrostatic unit of radiation (E unit).

The standard cell gave a deflection of 33.3.

Without the water-phantom the ionization chamber placed at the level where the rubber would be gave a deflection of 23.4 mm.

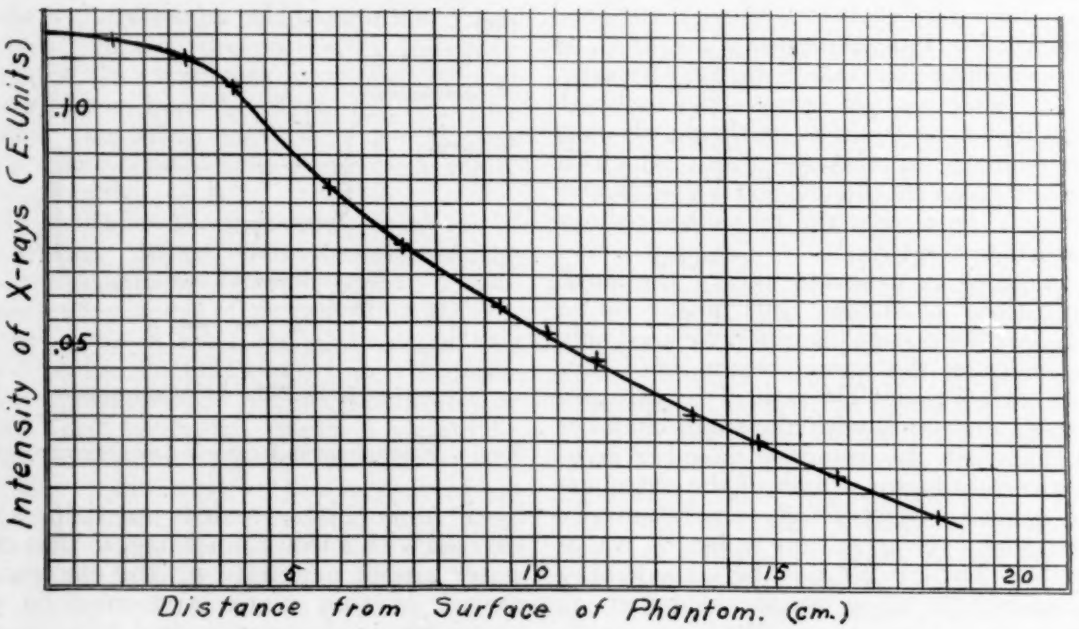

FIG. 3. Curve showing depth doses in a water-phantom.

The lead-covered wires leading to the ionization chamber, D, support it in any desired position in the water. In one experiment with this apparatus the following data has been obtained:

Current through *x*-ray tube—3 ma.

Rough estimate of voltage by sphere-gap—175 kv.

Effective wave-length measured by fraction of radiation passing through ½ mm. copper—0.16.

Distance from target to water-phantom —85 cm.

Depth of water—19.2 cm.

Portal of entry—20 × 20 cm.

The ionization chamber just below the rubber of the water-phantom gave a deflection of 34.5 mm. and the ionization chamber above the water in the phantom gave a deflection of 2.5 mm.

Thus, the intensity at the level where the rubber would be was $\frac{23.4}{33.3} \times 0.1 = 0.070E$ without the water-phantom.

On putting the water-phantom in place, the intensity rose to $\frac{34.5}{33.3} \times .1 = 0.104E$, representing an increase in intensity of about 49 per cent. This increase came from

the secondary radiation produced in the phantom.

The intensity just above the water in the phantom amounted to $\frac{2.5}{33.3} \times .1 = 0.0075$E, that is, approximately 7.3 per cent of that just below the phantom.

The following table contains the deflections and intensities of *x*-radiation at different distances above the under-surface of the rubber sheet:

Distances (cm.)	Deflection (mm.)	Intensity (E units)
1.3	38.0	.114
2.8	37.0	.111
3.8	34.5	.104
5.8	27.6	.083
7.3	23.5	.071
9.3	19.3	.058
10.3	17.5	.053
11.3	15.5	.047
13.3	12.0	.036
14.6	10.0	.030
16.3	7.8	.023
18.3	5.0	.015

The curve in Figure 3 has been drawn from the data of the above table and represents the decrease in intensity of *x*-rays on passing upward through the water in the phantom. It will be seen from the curve that the intensity at the surface of the rubber amounts to about 0.116E and at 10 cm. above the surface to about 0.054E. The percentage depth dose amounts, therefore, to 47 per cent at a depth of 10 cm. The curve is nearly horizontal for some distance above the surface of the phantom.

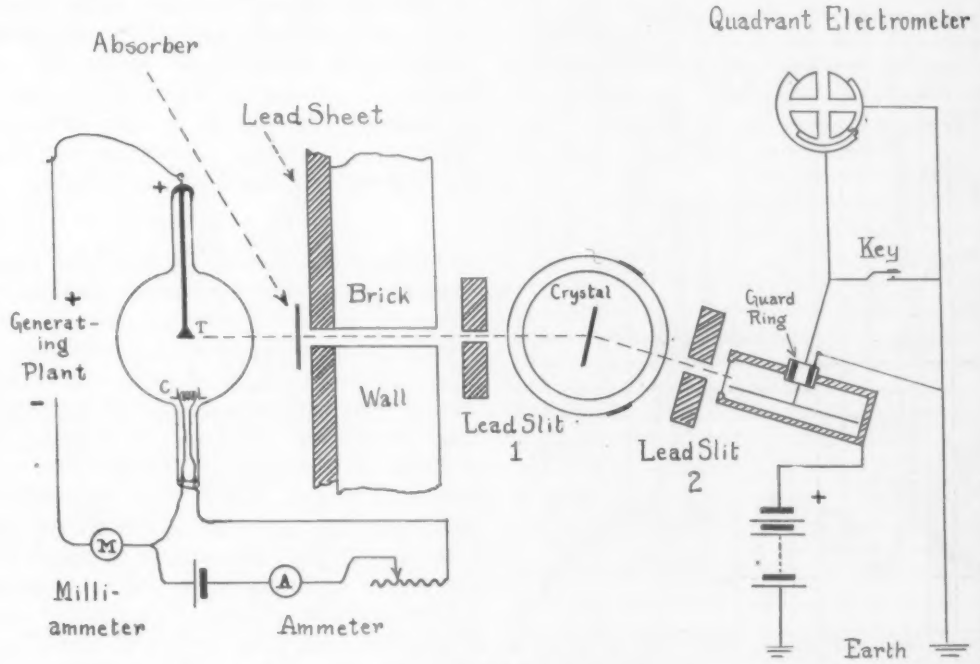

FIG. 4. Diagram of *x*-ray spectrometer.

THE WAVE-LENGTHS OF SCATTERED X-RAYS

Recent investigations of the distribution of intensity of *x*-radiation throughout water-phantoms, etc., have emphasized the importance of secondary and scattered *x*-rays. Perrin, in 1897, early in the history of *x*-rays, discovered the secondary radiation coming from substances on which *x*-rays fall. The question as to whether or not these secondary rays are as penetrating as the primary rays is one of great importance to the roentgenologist, not only on account of their influence on the distribution of radiation in a patient's body, but also from the point of view of the precautions that should be taken to protect the operator himself.

Recently, Dr. Clarke, Dr. Breit and the

writer have been investigating this problem by means of the *x*-ray spectrometer.[1] We have been studying the wave-lengths of the *x*-rays scattered from various substances. In general, short *x*-rays are more penetrating than longer ones. Further, the *x*-ray spectrometer furnishes us with the most accurate method of estimating the quality of radiation. Wave-lengths can be measured with far greater precision than

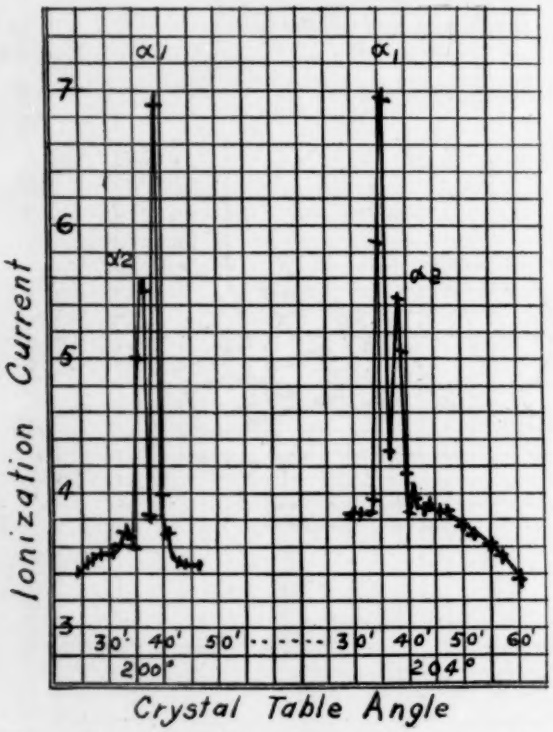

FIG. 5. The α lines in the spectrum of the *x*-rays coming directly from the target.

can absorption coefficients. As the following experiments indicate, we have found that the scattered radiation from a great variety of chemical elements contains a large amount of radiation of exactly the same wave-length as the primary rays. This means that the scattered radiation contains a large number of *x*-rays of the same penetration as the primary rays. The scattered radiation consists of longer waves than the primary, also; that is to say, *x*-rays of very much less penetration than the primary. But the fact that the scattered radiation contains a large amount of radiation of the same wave-length and penetration as the primary radiation means that corresponding precautions must be taken for the protection of the operator, etc.[1]

Our experiments on the secondary radiation consisted of two parts: In the first part we measured the wave-lengths of the *x*-rays coming from the tungsten target of the Coolidge *x*-ray tube.

Figure 4 represents the arrangement of the apparatus. The rays from the target T of the *x*-ray tube pass through a hole in a brick wall and then strike a crystal mounted on the table of the *x*-ray spectrometer. The planes in the crystal containing its atoms reflect *x*-rays having wave-lengths given by the formula

$$n\lambda = 2d \sin \theta,$$

according to Braggs' law. The reflected rays entering the ionization chamber represented in the figure produce a current which the quadrant electrometer measures. The curves in Figure 5 give the ionization currents at different angles of incidence, θ. The peaks on the curves represent the α lines in characteristic spectrum of the tungsten target. They have been measured on both sides of the zero of the instrument. The angles (half the angles measured from the peaks on one side to the corresponding peaks on the other) substituted in the above formula give for their wave-lengths the following values: for the peak α_1 λ = 0.209 and for the peak α_2 λ = 0.213 Ångströms.

In the second part of the experiment we measured the wave-lengths of the *x*-rays scattered from various materials. We employed exactly the same spectrometer set up in exactly the same way as in the first part of the experiment. We placed the *x*-ray tube in a vertical position, however, and shifted it to one side (as represented by Fig. 6) so that none of the rays coming from the tube could pass through the hole in the brick wall. As an additional precaution, a lead screen was placed between the tube and the first slit, as represented by A in Figure 6, so that none of the rays from the tube could strike the first lead slit. The substance

[1] For details see *Proc. Nat. Acad. Sc.*, Dec., 1923.

[1] See the researches by A. H. COMPTON, *Bull. Nat. Research Council*, Oct., 1922, p. 16; *Phys. Rev.*, May, 1923, p. 483 and June, 1923, p. 715.

producing the secondary rays was placed in line with the hole in the wall at B. With this arrangement of the apparatus the secondary rays from B alone could pass through the wall and enter the spectrometer. The readings of the spectrometer, therefore, measured the radiation given off from the substance B as secondary rays only.

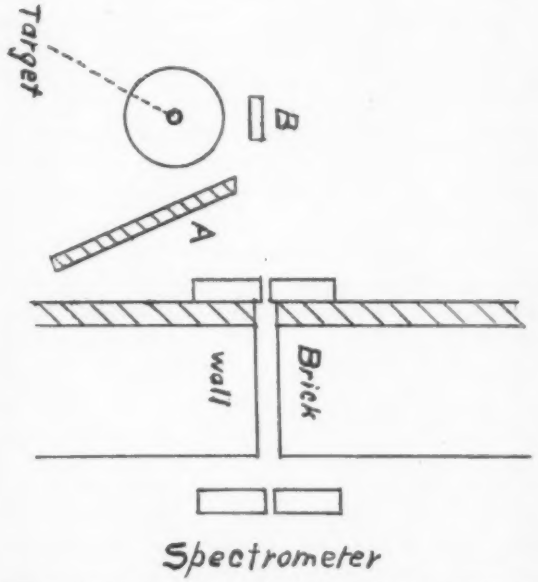

FIG. 6. Arrangement of tube and radiator for spectrum of scattered rays.

The curves in Figure 7 give the ionization currents for different positions of the crystal under these experimental conditions. We notice that the shapes of the curves are substantially the same as those in the first part of the experiment, although the peaks are not so completely separated from each other. In other words, the secondary radiation has substantially the same characteristics as the primary radiation. The peaks on the curves in Figure 7 occur at sensibly the same angles as those in Figure 5. Hence the wave-lengths, calculated from their positions by means of the above equation are, within the limits of error of measurements, the same as those of the primary rays. The secondary radiation, therefore, from the substance B (in this case carbon) contains a large amount of radiation of the same wave-length, i.e., of the same penetration, as the primary rays.

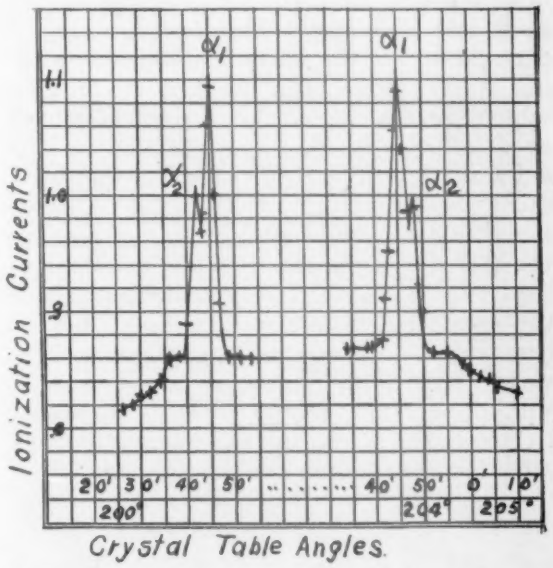

FIG. 7. The α lines in the spectrum of the x-rays scattered from carbon.

Similar results have been obtained for a variety of scattering substances containing chemical elements other than carbon—for instance, oxygen, aluminum, sulphur, potassium, copper, iodine, barium, lanthanium, praseodymium and neodymium.

THE ECONOMICS OF DOSIMETRY IN RADIOTHERAPY*

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AT PRESENT the mode of action of radiation on the cancer patient is practically unknown. Some maintain that the primary object of irradiation is to destroy the cancer tissue directly, while others assert that the destruction of the neoplasm is brought about indirectly by the reaction of the normal tissue surrounding it. Whatever the mechanism may be which brings about the regression and eventual disappearance of the tumor, it is evident that a certain dose of radiation must be administered to the patient, whether the tumor or any other part of the body be irradiated. It is for the clinician to decide what this dose shall be, and how the radiation should be distributed within the tissues. In general there are several ways of fulfilling his requirements, one of which, however, is the most economical. In the present paper experimental data are presented which enable the radiologist to determine the relative amount of radiation at any tissue depth for different conditions of treatment, and to administer it in the most economical way.

The progress of radiation therapy depends in a large measure on the judgment of the radiologist as to the results he obtains from treatments given under definite conditions. First of all, he must have a good knowledge of neoplasms and their natural course. Then he must be familiar with the accepted methods of treatment and the results obtained thereby. It is only then that he can form an idea of the efficacy of the particular treatments which he gives. This is really self-evident, and need not be discussed further. We shall assume that the radiologist possesses these requisites, and that, therefore, he is properly equipped to form a just estimate of the results which come under his observation. No radiologist, however, can be expected to draw the correct conclusions from previous treatments and use the information thus obtained as a guide in his present work, unless he can rely on his machine to deliver the same dose of radiation under the same conditions. The modern American *x*-ray machines, judiciously handled, are quite reliable in this respect, so that the handicap of uncertain radiation is not serious. In fact, it can be overcome entirely by taking the proper precautions. We may conclude, then, that the radiologist on whom the further development of radiation therapy depends, possesses the proper knowledge of cancer and has at his disposal a reliable source of radiation.

These requisites alone, however, will not lead to rapid progress. In addition the radiologist must have quantitative data which give him a rational basis for his treatments and clinical observations. What are the data which he needs? Our present knowledge does not permit a categorical answer to this question. We cannot say with certainty that some factors have no influence in bringing about the effects of radiation which we observe. Accordingly the logical thing to do is to give all the factors involved.

Of the physical factors involved the most important one is the distribution of the radiation in the tissue (normal as well as pathological). It is only when this is known for every treatment that the radiologist can form the proper criterion for effective dosage. The Germans have done a great deal of work along these lines, but little has been done in this country. Some charts have been published from time to time, but they are of limited applicability since they refer only to a definite set of conditions of treatment. In our work we needed distribution charts for different conditions of treatment (that is, different target-skin distances, filters and diaphragms) for our machine. We decided to determine these charts experimentally by ionization measurements.

The work of Friedrich showed that a very small ionization chamber made of organic materials must be employed. Since

* The authors of this paper were awarded second prize, 300.00, in the Leonard Prize contest.

no suitable instrument was available in this country, we proceeded to build one patterned after Friedrich's. We made some changes to increase the convenience of using such an instrument for a large number of measurements, but its essential features are the same as those of Friedrich's. It consists of a small ionization chamber made of clear bakelite, connected to a gold leaf electroscope by means of a rubber insulating cable. The electroscope is equipped with a projection device which enables the experimenter to observe the motion of the leaf on a ground glass screen instead of looking through a microscope. This arrangement reduces considerably the eyestrain when measurements have to be made for several hours continuously. The water-phantom is made of galvanized iron lined with wood 2 cm. thick, and is 30 cm. wide, 35 cm. long, and 30 cm. deep. It is equipped with a graduated screw so that the ionization chamber can be set at any height.

The information we wanted most urgently was for our deep therapy treatments, so the experiments were made with a machine operated at 200,000 volts crest value, and 4 ma. The voltage was determined in the following way: Keeping the milliamperes constant at 4 we measured the voltage *across the tube* by means of a sphere-gap constructed according to the Standardization Rules of the American Institute of Electrical Engineers, from the lowest point on the control to a maximum voltage of 210 kv. For each setting of the control handle we took many spark-gap readings quickly to eliminate as much as possible the effect of occasional surges. A voltmeter connected across the primary of the transformer was read at the same time. From the average of these readings the curve shown in Figure 1 was obtained. This relates the voltage applied to the tube to the primary voltage *when a current of 4 ma. flows through the tube.* The curve enables us to determine the impressed voltage for any setting by simply reading the primary voltmeter, *provided the current is 4 ma.* The advantage of this procedure lies not only in its simplicity but especially in its accuracy. The experimental points for the calibration curve are obtained by taking many readings for each setting. Then when an average curve is drawn we minimize errors still further.

With the machine set at 200,000 volts and 4 ma. we proceeded to determine depth dosage curves for 4 different diaphragms, 5 filters (3.67 mm. Al., 0.42, 0.84, 1.26, 1.68 mm. Cu.) and 2 target-skin distances (52.7 and 73.5 cm.). These

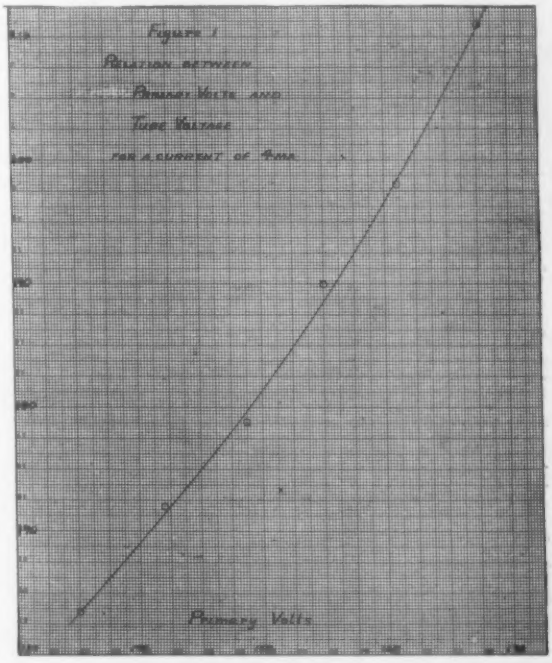

FIG. 1.

would give us 40 different dosage curves (central beam only) for various combinations of diaphragm, filter and distance. In tabulating the experimental data definite relations were discovered which lead to some useful generalizations. Before proceeding to the discussion of the results, however, we must mention the precautions which were taken in making the measurements.

With an instrument of this type several sources of error must be considered. (1) *The natural leak of the electroscope.* This has been quite constant during the last eighteen months. Since errors due to variations in the leakage have the

greatest effect on the longest readings taken, the natural leak was obtained always immediately after these readings. In the course of the day it was determined two or more times. The proper correction was then applied to all the readings. (2) *The effect of stray radiation on the electroscope and cable.* The electroscope is made of brass lined with 1 cm. of lead. The two windows are very small, one being 0.5 cm. and the other 1 cm. in diameter, and both are protected. The volume of the leaf house is small—4 × 4 × 1½ cm. Since the *x*-ray tube is practically enclosed in a lead-lined box, and the electroscope was always at a considerable distance from the tube, stray radiation had no appreciable effect on the electroscope. The possibility of ionization in the cable was considered and special tests were made to determine its magnitude. They showed that while the effect was present, it was negligible in our work. (3) *The "soaking" effect of the insulation.* This is always present in electroscope measurements, and it is very hard to correct for. We made a special test to determine what influence this had on electroscope readings varying in the ratio of 1:4 and found it to have no noticeable effect. We always charged the electroscope to the same point on the scale, and in the same manner. (4) *The effect of the cable on the amount of scattered radiation which reaches the ionization chamber.* An estimate of this was made by taking readings at different depths in the water-phantom with the ionization chamber as used ordinarily, and with a piece of cable held against its end. The addition of the cable-end decreased the ionization by about 4 per cent at a depth of 10 cm. in the phantom. At the surface the effect was not noticeable for filtered *x*-rays. (5) *The test for "saturation of the ionization chamber."* This was made by the use of radium. It was found that the electroscope readings were proportional to the amount of radium placed always in the same position relative to the ionization chamber, for a wider range of currents than that used in the experiments.

We shall now give the results of the experiments.

1. The Effect of the Size of the Field on the Amount of Radiation at Different Depths

Table I

EFFECT OF SIZE OF FIELD ON SURFACE RADIATION

200 kv. (crest value) 4 ma., 73.5 cm. T-S distance
Ionization chamber half submerged

Field, sq. cm.	Filter, in millimeters					Average for Filtered Rad.
	None	3.27 Al.	0.42 Cu.	0.84 Cu.	1.26 Cu.	
1000	100	100	100	100	100	100
237	95.2	92.3	92.6	92.0	90.6	91.9
118	90.9	86.5	86.8	87.0	86.2	86.6
41.5	84.0	79.4	79.0	78.8	78.7	79.0

The figures in Table I show that (*a*) the smaller the field the less the radiation effective at the surface; (*b*) the effect is substantially the same for the four filters shown; (*c*) a variation of the field from 1000 to 41.5 sq. cm. reduces the radiation by 21 per cent; (*d*) the effect is less marked for unfiltered rays. The same result was obtained with target-skin distances of 52.7 and 60.6 cm., and filters ranging from 3.27 mm. Al. to 1.68 mm. Cu.

Table II

EFFECT OF SIZE OF FIELD ON RADIATION AT 5 CM. DEPTH

200 kv. (crest value) 4 ma., 52.7 cm. T-S Distance

Field sq. cm.	Filter, in millimeters					Average for Cu. Filtered Rad.
	3.27 Al.	0.42 Cu.	0.84 Cu.	1.26 Cu.	1.68 Cu.	
1000	100	100	100	100	100	100
230	87.0	88.0	87.8	87.7	87.8	87.8
121	76.2	78.0	77.7	77.5	77.4	77.6
37.8	59.0	60.0	59.8	59.8	60.0	59.9

The figures of Table II show that (*a*) the smaller the field the less is the radiation effective at a depth of 5 cm.; (*b*) the effect is substantially the same for the 5 filters shown; (*c*) a variation of the field from 1000 to 37.8 sq. cm. reduces the radiation by 40 per cent. In this case also the same result was obtained with a distance of

73.5 cm. To avoid repetition we shall simply say that the same general conclusions apply to the radiation effective at a depth of 10 cm. Table III shows the results for one distance.

TABLE III

EFFECT OF SIZE OF FIELD ON RADIATION AT 10 CM. DEPTH

200 kv. (crest value) 4 ma., 52.7 cm. T-S Distance

Field sq. cm.	Filter, in millimeters					Average for Cu. Filtered Rad.
	3.27 Al.	0.42 Cu.	0.84 Cu.	1.26 Cu.	1.68 Cu.	
1000	100	100	100	100	100	100
230	82.3	82.0	81.0	81.5	81.8	81.8
121	70.0	68.6	68.7	68.5	68.5	68.6
37.8	48.1	49.4	49.6	48.9	49.3	49.3

We are anxious not to convey a wrong impression by the wording of this generalization. We wish to call particular attention, therefore, to the limits of its applicability. The experimental data on which it is based covered the following ranges: Distance, 52.7 to 73.5 cm.; filter, 0.42 mm. Cu. to 1.68 mm. Cu., also 3.27 mm. Al.; skin area, 40 sq. cm. to 1000 sq. cm., the fields being rectangular with sides approximately in the ratio of 7:10; water depth, 0 to 10 cm. in the phantom already described. In addition, several special experiments were made to extend the range of the skin areas down to 20 sq. cm. and the range of the tissue depth to 15 cm. Within these limits for the different factors, therefore, the above generalization holds with a considerable degree of accuracy. That the limits can be extended somewhat on either side without introducing a large error can be readily granted. The final results are shown graphically in Figure 2. This supplies the necessary quantitative data to make the proper corrections in the dose according to the size of the skin area irradiated.

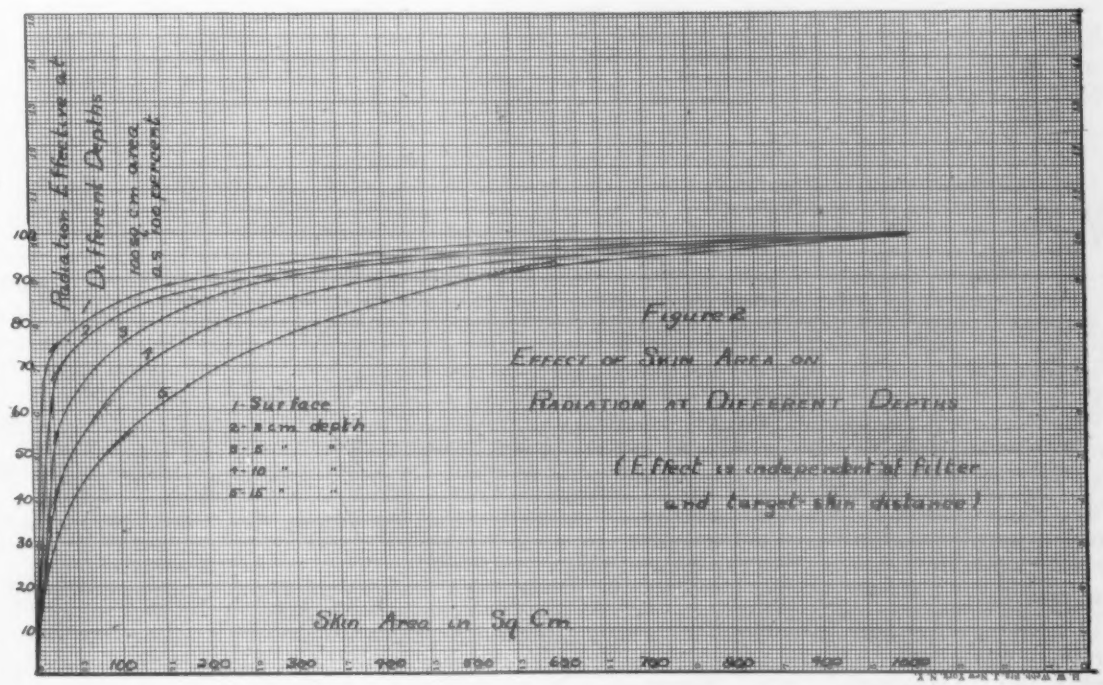
Radiation Effective at Different Depths
as % of 100 sq. cm. area
1 Surface
2- 5 cm. depth
3- 5 " "
4- 10 " "
5- 15 " "
Figure 2
Effect of Skin Area on
Radiation at Different Depths
(Effect is independent of filter and target-skin distance)
Skin Area in Sq. Cm.

FIG. 2.

We may make now the first generalization:

A. The effect of the size of the field on the radiation effective at any particular tissue depth is the same for all filters and all distances used in practice.

2. The Effect of the Filter on the Amount of Radiation Effective at Different Depths

Table IV

EFFECT OF FILTER ON SURFACE RADIATION

200 kv. (crest value) 4 ma., 73.5 cm. T-S Distance
Ionization Chamber Half Submerged

Copper Filter mm.	Area on Surface of Water, in sq. cm.				Average
	41.5	118	237	1000	
0	412	405	397	387	400
0.42	100	100	100	100	100
0.84	64.7	64.8	64.0	64.5	64.5
1.26	48.2	47.8	47.0	48.2	47.8

The figures given in Table IV show that the influence of the filter on the radiation effective at the surface is practically the same for fields ranging from 41.5 to 1000 sq. cm. when the surface of the water is 73.5 cm. from the target. The only considerable variation occurs for unfiltered radiation. This is probably due to the fact that the electroscope readings in this case were very short and therefore not very reliable. Since unfiltered radiation at this voltage is of no particular interest to us, no attempt was made to check the results. They are given here because they will serve as a guide in plotting the curve to represent the results graphically. The values for 3.27 mm. Al. were also obtained, but they are of little if any practical value and are omitted from the table. A similar agreement among the percentages for the four copper filters was obtained with a distance of 52.7 cm. and four different areas. Furthermore the percentages are essentially the same for the two distances. From this we may conclude that the effect of the filter on the surface radiation is independent of the irradiated area and the target-skin distance.

Tables V and VI show the influence of the filter on the radiation effective at a 5 cm. and 10 cm. depth respectively, for a distance of 52.7 cm. It will be seen that here also the relative effect of the filter is independent of the size of the irradiated area.

Table V

EFFECT OF FILTER ON RADIATION AT 5 CM. DEPTH

200 kv. (crest value) 4 ma., 52.7 cm. T-S Distance

Copper, mm.	Area on Surface of Water, in sq. cm.				Average
	37.8	121	230	1000	
0	232	227	221	214	224
0.42	100	100	100	100	100
0.84	66.7	66.7	66.7	66.7	66.7
1.26	49.7	49.7	49.8	51.2	49.7
1.68	38.3	39.2	38.5	39.3	38.8

Table VI

EFFECT OF FILTER ON RADIATION AT 10 CM. DEPTH

200 kv. (crest value) 4 ma., 52.7 cm. T-S Distance

Copper, mm.	Area on Surface of Water				Average
	37.8	121	230	1000	
0	176	189	176	186	181
0.42	100	100	100	100	100
0.84	68.4	70.2	69.5	70.2	70.0
1.26	51.8	53.2	53.2	53.3	53.2
1.68	42.3	43.2	41.8	42.8	42.3

It is hardly necessary to give the complete results for the determination at a 73.5 cm. distance. The average values obtained with three copper filters, however, are shown in Table VII.

Table VII

EFFECT OF FILTER ON RADIATION AT 5 AND 10 CM. DEPTH

200 kv. (crest value) 4 ma., 73.5 cm. T-S Distance

Copper, mm.	Average for all Fields Employed	
	5 cm. Depth	10 cm. Depth
0.42	100	100
0.84	67.4	71.4
1.26	49.5	54.9

The agreement between these values and the corresponding ones for the 52.7 cm. distance is not as good as in the previous cases. However it should be remembered that measurements at a 10 or even at a 5 cm. depth with a filter of 1.26 mm. of

copper when the distance is 73.5 cm., are rather difficult, on account of the small amount of radiation reaching the ionization chamber. The maximum variation shown in Tables VI and VII occurs for the 1.26 mm. filter and is $\frac{54.9 - 53.2}{53.2} = 3$ per cent. It is not unreasonable, therefore, to attribute this to the inherent difficulty of the experiments at 73.5 cm. distance. Bearing in mind the practical applications of this work we are justified in making the second generalization.

We may summarize the results presented so far by saying that the relative effects of the field of radiation and the filter are independent of each other and that both are independent of the target-skin distance.

3. The Effect of the Target-skin Distance on the Amount of Radiation at Different Depths

Figure 4 shows two dosage curves for the following conditions of treatment: A is for a target-skin distance of 52.7 cm.,

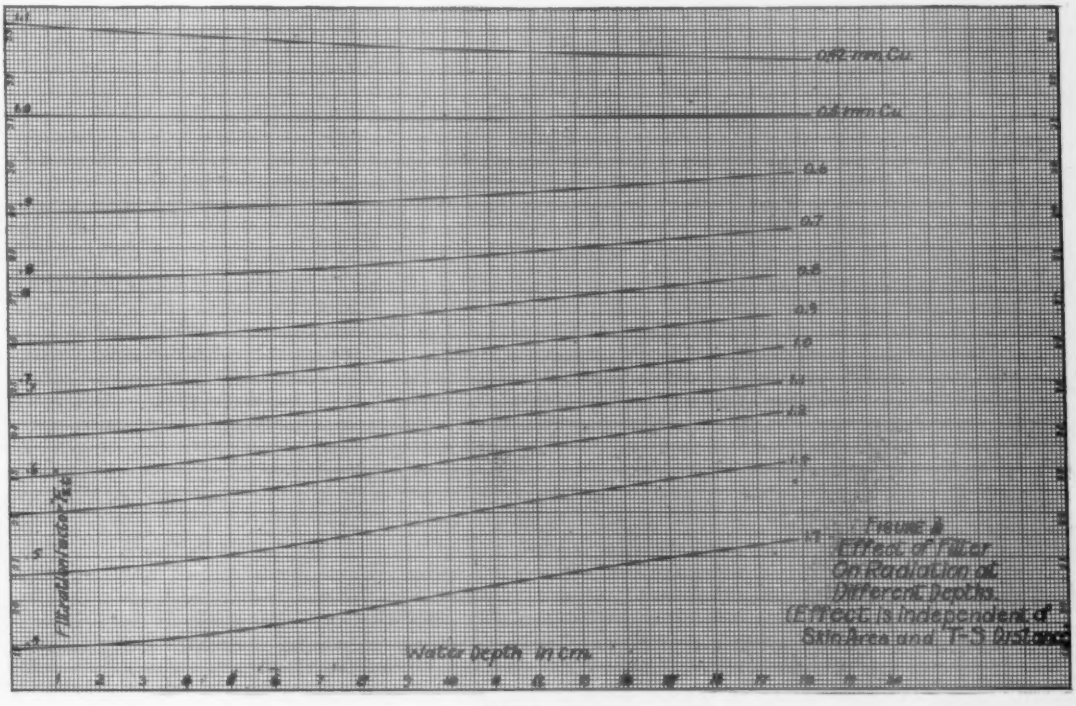

Fig. 3.

B. *The effect of the filter on radiation at any particular tissue depth is the same for all skin areas and all distances used in practice.*

The limitations of this generalization are similar to those for Generalization A and need not be discussed further. The range for tissue depths was extended to 15 cm. by subsidiary experiments. (The graphical representation of the results is shown in Figure 3, which will be explained later).

B for 73.5 cm. In both cases the filter is 0.42 mm. Cu., the skin area 120 sq. cm. (The voltage for all the data given in this paper is for 200,000 volts crest value). The curves show the effect on the relative depth doses of a change in distance from 52.7 to 73.5, the other conditions remaining the same. It will be seen that the difference in the depth dose at 10 cm. is from 34.2 per cent for the shorter distance to 37.9 for the longer one.

TABLE VIII

200 KV. (CREST VALUE) 0.42 MM. Cu. FILTER 120 SQ. CM. FIELD

A	B	C	D	E	F	G
Depth, cm.	52.7 cm. Distance Per Cent Surface Radiation			73.5 cm. Distance Per Cent Surface Radiation		
	Meas.	Inv. Sq.	Ratio B/C	Meas.	Inv. Sq.	Ratio E/F
0	100	100	1.00	100	100	1.00
1	100	96.3	1.038	100	97.2	1.029
2	93.8	92.8	1.010	96.8	94.7	1.022
3	85.7	89.5	0.958	88.3	92.3	0.959
4	76.7	86.4	0.888	80.0	90.0	0.890
5	68.1	83.4	0.818	72.0	87.6	0.822
6	60.0	80.7	0.744	63.9	85.5	0.746
7	52.3	77.9	0.671	56.5	83.4	0.678
8	45.5	75.4	0.602	49.5	81.3	0.610
10	34.2	70.7	0.483	37.9	77.4	0.490
12	25.5	66.3	0.385	28.6	73.8	0.391
15	17.0	60.6	0.281	19.7	69.0	0.286

Since in the two curves the only factor which is different is the target-skin distance, we may reasonably expect the effect of the distance to depend on the inverse square law. In Table VIII we have listed the percentages read from the above curves and the percentages calculated by means of the inverse square law alone, for the two distances respectively. The equation is:

Percentage of Surface Radiation $= 100\frac{X^2}{(X+Z)^2}$

where x is the target-skin distance (52.7 or 73.5 cm. as the case may be) and z is the water depth (from 0 to 15 cm.). Taking the ratio between the experimental values and the values calculated from the above equation for each depth and the two distances we obtain the values shown in columns D and G. It will be seen that the agreement between the values for the two distances is quite close. The maximum variation occurs at the 15 cm. depth where the difference is less than 2 per cent. In order to make sure that the close agreement is not accidental we looked up Dessauer's[1] data and found even a better agreement. This is shown in Table IX. Here the ratios agree almost exactly for a range of target-skin distances from 30 cm. to 70 cm.[2] The better agreement is probably due to the fact that Dessauer's values for the different distances are referred to the same *volume* of water, whereas ours are for the same irradiated areas. Our data for the effect of the field (Fig. 2) enables us to make this correction and in that case the agreement is very close. Since, however, the error is small if the target-skin distances are not very different, we may neglect this factor. Dessauer's data shows also that the same general relation holds for different voltages and filters. (The ratios, of course, are different in each case.) This permits us to make the third generalization:

C. *If all the dosage factors except the target-skin distance are the same, the relative depth doses depend only on the inverse square law.*

TABLE IX

Depth, cm.	Target-skin Distance														
	30 cm.			40 cm.			50 cm.			60 cm.			70 cm.		
	Dess.	Inv. Sq.	Ratio	Dess.	Inv. Sq.	Ratio	Dess.	Inv. Sq.	Ratio	Dess.	Inv. Sq.	Ratio	Dess.	Inv. Sq.	Ratio
0	100	100	1.00	100	100	1.00	100	100	1.00	100	100	1.00	100	100	1.00
5	70.2	73.6	1.05	75.1	78.8	1.05	78.6	82.7	1.05	81.5	85.1	1.05	83.0	87.0	1.05
10	47.5	56.3	1.18	54.2	63.9	1.18	59.0	69.5	1.18	62.3	73.5	1.18	64.6	76.5	1.18
15	29.0	44.5	1.54	34.8	52.8	1.52	39.2	59.2	1.51	41.5	63.9	1.54	45.0	67.8	1.51

This is strictly true only when the same volume is irradiated at the distances considered. If the same skin area is maintained a small error is introduced for depths from 0 to 15 cm. We prefer to refer our data to the same skin areas, however, because this is simpler from the standpoint of the radiologist.

Having one curve of the type shown in Figure 4, for a definite set of dosage

[1] DESSAUER u. VIERHEELER. *Strahlentherapie*, xii, Heft 3, Seite 655.

[2] DESSAUER'S ratios cannot be expected to agree with those of Table VIII because the skin area and the filter in the two cases are very different.

factors, Generalization C permits us to calculate similar curves for other distances, provided the remaining factors are the same. To make this clearer we shall take the data given in Table VIII for a 52.7 cm. distance and calculate the relative depth doses for a 73.5 cm. distance when the filter and skin area are the same as for the 52.7 cm. distance. The ratio in Column D will be assumed to apply to the 73.5 cm. distance, and all that is necessary is to multiply the inverse square law values for the different depths at the new distance by the corresponding ratios. This is shown in Table X. The experimental values for the 73.5 cm. distance are also given to show that the error introduced by our assumption is negligible.

TABLE X

Depth, cm.	73.5 cm. Distance			
	Ratio for 52.7 cm.	Inv. Sq. Law Value	Calculated Per Cent	Experimental Per Cent
0	1.00	100	100	100
2	1.01	94.8	95.6	96.8
4	0.868	89.8	78.0	80.0
7	0.671	83.3	56.0	56.6
10	0.484	77.5	37.5	37.9
15	0.281	68.9	19.4	19.7

In a similar way we can calculate curves for other distances. To minimize errors it is best to use the ratios for the 52.7 cm. distance for distances smaller than 50 cm. and the ratios for the 73.5 cm. distance for distances greater than 70 cm. For a distance of 60 cm. average values will be best. In general, however, we may take the average of the two ratios without introducing a serious error in the calculated depth doses for all target-skin distances used in practice.[1]

The combination of the three generalizations and the curves given so far enables us to calculate the depth doses *in percentage of the surface dose* for any target-skin distance, any skin area, and any filter used in practice (the voltage being 200 kv. crest value). The radiologist, however, must know also how to administer a skin dose under various conditions of treatment. For this purpose additional information is required.

[1] A method of calculation similar to this is given by Dessauer. Ours is somewhat simpler because the same set of ratios applies to every distance. The same relation can be derived from Dessauer's data, although the ratios will be different.

4. The Applicability of the Inverse Square Law for Skin Dosage

From time to time we have seen in the literature articles relating to the validity of the inverse square law. It should be

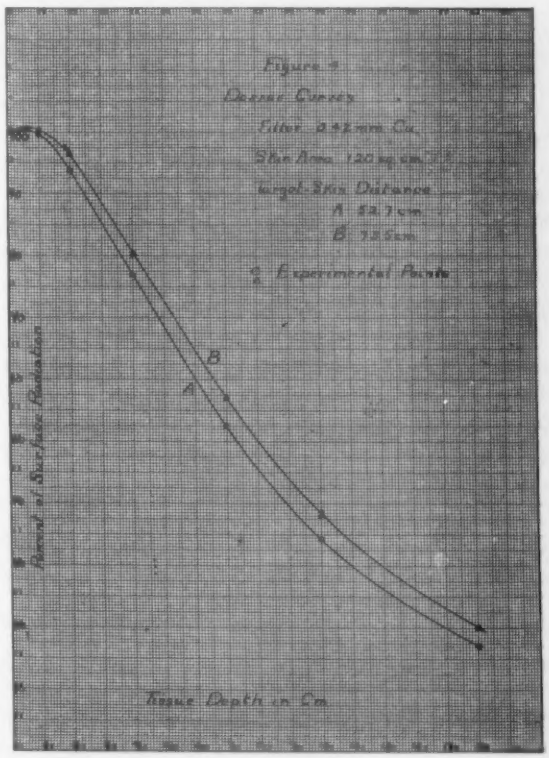

FIG. 4.

remembered that this "law" is simply a geometrical relation which must necessarily hold for radiation emitted by a point source and traveling in straight lines. The only question to consider, therefore, is whether the conditions met with in radiotherapy justify the application of the inverse square law. It will be readily seen that the source of radiation is not strictly a point source and that the interposition of a filter changes the path of the rays to a certain extent, through scattering and the production of secondary radiation. Furthermore, the effect on the skin, which is principally what concerns us in this connection,

depends not only on the amount of radiation falling thereupon, but also on the amount of radiation scattered backward by the underlying tissue. We may conclude a priori, therefore, that the inverse square law is not strictly applicable to our problem.

We made experiments to determine the variation of the surface radiation with the target-skin distance under various conditions of filter and irradiated area. In this work we employed also the small ionization chamber, since this would give us the most accurate information. The procedure was as follows: Readings were taken with the ionization chamber at different distances from the tube with several diaphragms and filters. In one set of experiments the chamber was supported in air and in another it was placed on the surface of the water in the phantom. We chose the half-submerged position of the chamber, since this is the position ordinarily taken for the zero depth in such measurements.[1] The data given in Table XI show that the inverse square law can be used to calculate skin doses for different distances *provided the same beam of radiation is maintained.* That is, provided the *same diaphragm* placed at the *same distance* from the tube is used for all distances. If the diaphragm is adjusted to give the same irradiated area at the different distances the inverse square law is not longer applicable.

This is evident from the fact that the surface radiation is influenced by the size of the field and that the above condition of a fixed beam of radiation requires different areas at different distances (varying as the square of the distance).

The experiments with the ionization chamber in air (without water backing) gave the same results. That is, the inverse square law is applicable only when the same beam of radiation is measured at different distances, but not when the size of the *diaphragm* is changed from one distance to another. We found that, at the same distance, the larger diaphragm gave the larger ionization current, even though there was nothing below the ionization chamber which would scatter radiation back into it. (The wooden floor was more than one meter below the ionization chamber.) We had previously tested the cable for ionization and found it negligible, but in order to make sure that the effect was not due to radiation scattered by the cable into the chamber, we covered with lead the part exposed to the rays. This made no difference in the results. We concluded, therefore, that the increase in the ionization current with a larger diaphragm was due to the larger amount of radiation scattered by the filter when the cross-section of the beam was larger. This conclusion is substantiated by the observation that the ionization chamber registers a larger current when the filter is brought closer to it, even though other conditions remain the same. (This observation was made also by Friedrich.) Accordingly in this work it is important to specify the position of the filter. In all our experiments both the filter and the diaphragm were placed at a distance of 40 cm. from the target.

The results of these experiments enable us to make the fourth generalization:

D. *For purposes of Skin Dosage in Radiotherapy, the inverse square law is applicable, provided the same beam of radiation is effective at the different distances considered.*

This generalization permits us to calculate the proper dose to administer when we vary the target-skin distance, provided

TABLE XI

Ionization Chamber Half-submerged in Water Phantom. Diaphragm and Filter Placed at 40 cm. from Target

Distance Target cm.	Filter, in mm.			Average for all Filters	Calculated by Inverse Square Law
	3.27 Al.	0.42 Cu.	0.84 Cu.		
5 by 7 cm. Diaphragm					
50.9	100	100	100	100	100
60.6	71.3	71.9	70.2	71.3	70.6
73.5	46.7	48.8	48.2	47.9	47.8
7 by 10 cm. Diaphragm					
50.9	100	100	100	100	100
60.6	70.4	70.2	71.8	70.8	70.6
73.5	47.4	48.5	48.8	48.2	47.8

[1] For the effect of the zero position for the ionization chamber see WEATHERWAX and LEDDY, AM. J. ROENTGENOL., June, 1923, x, No. 6, p. 488.

we know the dose for one distance and we use always the same diaphragm. In practice, however, it is necessary to adjust the size of the beam of radiation to the requirements of the case under treatment. For this purpose the inverse square law alone does not suffice. We can, however, work out correction factors which enable us to calculate the proper dose for any distance and any skin area. Going back to Generalization A we see that the effect of the size of the field on the surface radiation (zero depth) is the same for all practical distances. If a beam of radiation has a cross-section of 100 sq. cm. at a distance of 50 cm. from the target, the areas at other distances are as shown in Table XII.

TABLE XII

Distance, cm.	Area, sq. cm.
30	36
40	64
50	100
60	144
70	196
80	256
100	400

Hence if we know the skin dose for any one of these areas and the corresponding distance, the inverse square law determines it for all the other distances and the corresponding areas. Let us say, however, that we wish to know the amount of radiation effective at the center of a skin area of 100 sq. cm. at 70 cm. distance. Taking the radiation for a field of 100 sq. cm. at 50 cm. as unity, we determine by means of the inverse square law that the radiation from a field of 196 sq. cm. at 70 cm. is $1 \times \frac{50^2}{70^2}$ or 51 per cent. For an area of 100 sq. cm. it will be less than this, and Figure 2 enables us to obtain the proper value. Thus for an area of 196 sq. cm. the value from the proper curve in Figure 2 is 90, and for 100 sq. cm. it is 84.4. Hence the radiation effective at the center of an irradiated area of 100 sq. cm. at a distance of 70 cm. is $\frac{84.4}{90} \times 51 = 47.8$ per cent of that at 50 cm. with 100 sq. cm. area. The ratio $\frac{84.4}{90} = 0.938$ then, is the factor by which the inverse square law value of the radiation must be multiplied to obtain the correct amount for a field of 100 sq. cm. at 70 cm. In the same manner we can calculate the correction factors for the other distances. Such factors are given in Table XIII covering a wide range of distances and skin areas. They are all based on the value for each area at 50 cm. as unity.

5. The Development of an Equation for the Calculation of Doses at Different Depths, under Different Conditions of Treatment

The results of our experiments presented so far are accompanied by quantitative data which enable us to calculate the relative amount of radiation effective at any tissue depth for all practical conditions of treatment (the voltage being 200 kv. crest value). The process of calculation, however, is rather involved. To overcome this difficulty we have worked out an equation which reduces the process to one of simple substitution of the proper values for the factors involved. We shall explain this briefly. We have assumed as our unit the radiation required to produce a skin erythema at a distance of 50 cm. with a field of 100 sq. cm. and a filter of 0.5 mm. Cu. placed at a distance of 40 cm. from the target, the voltage being 200 kv. (crest value). It will be noticed that we do not state what constitutes an erythema, for this is immaterial as far as the values obtained from this equation are concerned. They will all be relative to whatever degree of erythema the radiologist wishes to adopt as his standard. This and the machine which he uses will determine the milliampere-minutes which will produce the standard erythema under the conditions specified above. The dosage curve for the standard conditions adopted is shown in Figure 5; the percentages read from this curve are listed in Column B of Table XIV. The percentages obtained by using the inverse square law are given in Column C. The ratios between the two appear in Column D. According to Generalization C these factors enable us to calculate the

TABLE XIII

BEAM AREA FACTORS b_{XA}

T-S Distance, X = cm.	Area of Skin Irridiated, Square Centimeters											
	A = 25	A = 50	A = 75	A = 100	A = 150	A = 200	A = 300	A = 400	A = 500	A = 600	A = 800	A = 1000
35	1.075	1.075	1.072	1.086	1.068	1.067	1.067	1.059	1.057	1.052	1.040	1.031
40	1.053	1.049	1.048	1.045	1.045	1.042	1.038	1.037	1.033	1.030	1.020	1.016
50	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
60	0.958	0.963	0.963	0.967	0.967	0.971	0.972	0.978	0.982	0.987	0.995	
70	0.929	0.936	0.936	0.937	0.943	0.946	0.954	0.966	0.972	0.977	0.990	
80	0.883	0.915	0.916	0.918	0.923	0.929	0.942	0.958	0.962	0.968	0.981	
100	0.868	0.876	0.878	0.885	0.897	0.910	0.936	0.951	0.954	0.960	0.971	

TABLE XIV

200 kv. (Crest Value) 50 cm. T-S Distance
100 sq. cm. Field 0.5 mm. Cu. Filter (40 cm. from Target)

Tissue Depth, cm.	Experimental Values	Inverse Square Law Values	Ratio b/c = R_z
A	B	C	D
0	100	100	.100
1	100	96.1	1.04
2	93.5	92.4	1.011
3	85.4	89.0	0.960
4	75.1	85.7	0.876
5	67.4	82.7	0.815
6	59.1	79.7	0.742
7	51.2	76.8	0.667
8	44.5	74.3	0.599
10	33.2	69.4	0.478
12	24.7	65.0	0.380
15	16.6	59.2	0.281

TABLE XV

VALUES OF R_Z

Tissue Depth, Z cm.	x = 50	x = 70	Average
0	1.00	1.00	1.00
1	1.04	1.03	1.035
2	1.011	1.006	1.008
3	0.96	0.945	0.952
4	0.876	0.870	0.873
5	0.815	0.803	0.809
6	0.742	0.730	0.736
7	0.667	0.657	0.663
8	0.599	0.582	0.590
9	0.537	0.520	0.529
10	0.478	0.467	0.472
12	0.380	0.368	0.374
15	0.281	0.267	0.274
18	0.193	0.180	0.186

percentages for any other distance provided the filter and the size of the field remain constant. Therefore for a field of

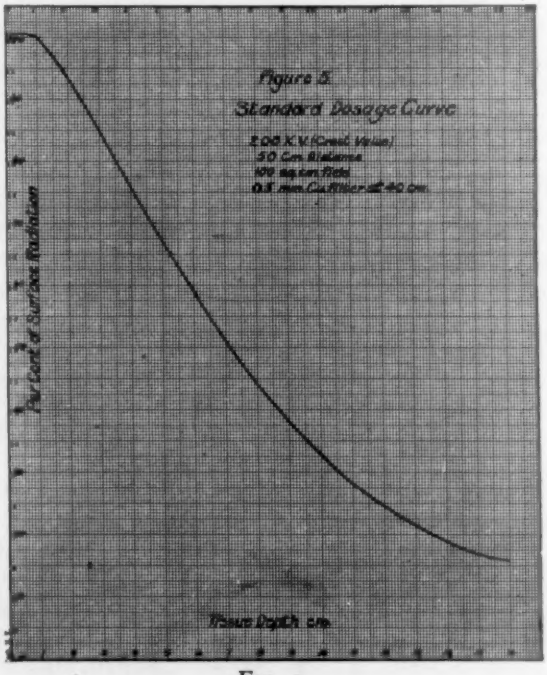
Figure 5.
Standard Dosage Curve
200 K.V. (Crest Value)
50 Cm. T-S Distance
100 sq. cm. Field
0.5 mm. Cu. Filter at 40 cm.
Per Cent of Surface Radiation
Tissue Depth cm.

FIG. 5.

100 sq. cm. and a filter of 0.5 mm. of copper, the radiation effective at any depth Z is

$$R = 100 \frac{X^2}{(X+Z)^2} r_Z$$

where x is the target-skin distance in cms.
Z is the tissue depth in cms.
r_Z is a factor whose values for different tissue depths Z are listed in Column D of Table XIV, and for more general conditions, in Table XV.

Thus, if we wish to calculate the relative radiation effective at a depth of 10 cm. when the target-skin distance is 70 cm., the field 100 sq. cm. and the filter 0.5 mm. Cu., we have $R = 100 \frac{(70)^2}{(70+10)^2} \times 0.478 = 36.6$ per cent of the surface radiation at 70 cm. (0.478 is the value of r_Z in Table XV corresponding to Z = 10 cm.).

For our purposes it is more convenient to express the results in terms of the unit defined above (50 cm. distance, 0.5 mm. Cu. filter, 100 sq. cm. field). The equation then becomes

$$R = \frac{50^2}{(X+Z)^2} r_Z \; b_{XA} \; a_{ZA}$$

where b_{XA} is a correction factor which takes account of the change in the beam of radiation when we maintain the same skin area at all distances. The subscripts X and A indicate that its value depends on the target-skin distance and the irradiated area.

a_{ZA} is the skin area factor which takes account of the effect of the size of the field at the 50 cm. distance. The subscripts Z and A indicate that its value depends on the tissue depth and the irradiated area.

Values of b_{XA} for different distances and different skin areas are given in Table XIII. Values of a_{ZA} for different skin areas and different tissue depths are listed in Table XVI.

This equation enables us to calculate the radiation effective at any tissue depth (0 to 18 cm.) for any target-skin distance and any size of field used in practice, but only for a filter of 0.5 mm. Cu. Our data for the effect of the filter on the radiation at different tissue depths enables us to enlarge the scope of the equation by the introduction of an additional factor f_{Zt} (the subscripts Z and t indicate that the values of this factor depend on the tissue depth and thickness of the copper filter). Values for different tissue depths and various copper filters are given in Table XVII. The final equation then becomes:

$$R = \frac{50^2}{(X+Z)^2} r_Z \; b_{XA} \; a_{ZA} \; f_{Zt}$$

Let us work out a few examples. What is the amount of radiation effective at a depth of 10 cm. if we use a target-skin distance of 50 cm., a filter of 1.0 mm. Cu. and a field of 400 sq. cm.?

$X = 50, Z = 10, r_{10} = 0.478$ (from Table XV)

TABLE XVI

EFFECT OF DIAPHRAGM AT DIFFERENT DEPTHS

Values of skin area factors a_{ZA}

Depth, cm. Z	Square Centimeter Area on Skin											
	A = 25	A = 50	A = 75	A = 100	A = 150	A = 200	A = 300	A = 400	A = 500	A = 600	A = 800	A = 1000
0	0.869	0.935	0.970	1.00	1.040	1.060	1.105	1.130	1.150	1.160	1.170	1.180
1	0.852	0.928	0.968	1.00	1.042	1.066	1.112	1.135	1.155	1.168	1.180	1.194
2	0.824	0.914	0.963	1.00	1.050	1.080	1.120	1.150	1.170	1.180	1.200	1.220
3	0.790	0.890	0.952	1.00	1.066	1.104	1.144	1.180	1.198	1.212	1.235	1.258
4	0.757	0.868	0.940	1.00	1.080	1.130	1.178	1.215	1.232	1.250	1.278	1.302
5	0.725	0.853	0.933	1.00	1.090	1.150	1.210	1.250	1.270	1.290	1.320	1.340
6	0.704	0.840	0.928	1.00	1.098	1.162	1.233	1.280	1.298	1.330	1.354	1.380
7	0.684	0.830	0.924	1.00	1.104	1.176	1.254	1.306	1.327	1.360	1.390	1.416
8	0.664	0.820	0.920	1.00	1.110	1.188	1.275	1.333	1.358	1.395	1.425	1.458
9	0.650	0.810	0.918	1.00	1.114	1.198	1.298	1.360	1.390	1.428	1.462	1.498
10	0.638	0.800	0.916	1.00	1.120	1.200	1.320	1.390	1.430	1.460	1.500	1.540
12	0.618	0.792	0.912	1.00	1.128	1.224	1.372	1.460	1.514	1.560	1.610	1.656
15	0.598	0.786	0.908	1.00	1.140	1.270	1.460	1.590	1.680	1.740	1.820	1.870
18	0.580	0.780	0.898	1.00	1.154	1.318	1.575	1.754	1.908			

$b_{50,400} = 1$ (from Table XIII) $a_{10,400} = 1.39$ (from Table XVI)
$f_{10.1} = 0.687$ (from Table XVII)
Hence

$$R = \frac{50^2}{(50+10)^2} \times 0.478 \times 1.39 \times 0.687 = 0.317$$

That is, the radiation at 10 cm. depth under the conditions of the problem is 31.7 per cent of the unit we have adopted. If we desire the percentage depth dose we have to divide the value obtained by the surface radiation effective under the same conditions. This is

$$R = \frac{50^2}{(50+0)^2} \times 1 \times 1 \times 1.13 \times 0.635 = 0.718$$

or 71.8 per cent of the unit we have adopted. Therefore, the percentage depth dose for the conditions of the problem is $\frac{0.317}{0.718} = 44.1$ per cent.

In this problem we have selected the conditions which are usually given for comparison in American literature (distance 50 cm., field 20 × 20 cm. = 400 sq. cm., filter = 1.0 mm. Cu.). It will be seen that the value of 44.1 per cent for the dose at 10 cm. depth is in good agreement with the values reported by other investigators working with machines of different makes. From Bachem's report (Bachem. *J. Radiol.*, June, 1923, iv, No. 6) we may take 42 per cent as the average depth dose for American machines under the conditions specified above. If our results had not been corrected for the effect of the cable in shutting off some radiation from the ionization chamber, our percentage for these conditions would also be 42. This correction, to our knowledge, has not been made by other experimenters. It is very likely, therefore, that the difference is only apparent and not real.

Let us take another example. Determine the percentage radiation at a depth of 8 cm. under the following conditions: Target-skin distance 70 cm., filter 1.2 mm. Cu., field 300 sq. cm. Here X = 70, Z = 8, $r_8 = 0.582$ (from Table XV) $b_{70,300} = 1.047$ (from Table XIII) $a_{8,300} = 1.275$ (from Table XVI) $f_{8,\ 1.2} = 0.594$ (from Table XVII). Therefore

$$R = \frac{50^2}{(70+8)^2} \times 0.582 \times 1.047 \times 1.275 \times 0.594 = 0.181$$

or 18.1 per cent of our unit.
For the surface radiation X = 70, Z = 0,

TABLE XVII
EFFECT OF FILTERS AT DIFFERENT DEPTHS
Values of filtration factors f_{Zt}

Depth, cm. Z	Mm. Copper										
	ft. = 0.42	ft. = 0.5	ft. = 0.6	ft. = 0.7	ft. = 0.8	ft. = 0.9	ft. = 1.0	ft. = 1.1	ft. = 1.2	ft. = 1.5	ft. = 1.7
0	1.111	1.00	0.890	0.808	0.740	0.684	0.635	0.590	0.548	0.480	0.397
1	1.107	1.00	0.891	0.810	0.742	0.686	0.637	0.593	0.550	0.482	0.399
2	1.100	1.00	0.892	0.812	0.744	0.688	0.639	0.596	0.553	0.484	0.400
3	1.096	1.00	0.893	0.814	0.746	0.692	0.643	0.600	0.558	0.489	0.404
4	1.093	1.00	0.895	0.817	0.749	0.697	0.648	0.606	0.564	0.494	0.408
5	1.090	1.00	0.897	0.820	0.755	0.702	0.653	0.612	0.571	0.502	0.416
6	1.088	1.00	0.899	0.824	0.760	0.708	0.658	0.619	0.578	0.510	0.424
7	1.086	1.00	0.902	0.828	0.765	0.714	0.664	0.626	0.586	0.519	0.432
8	1.084	1.00	0.904	0.832	0.770	0.720	0.671	0.634	0.594	0.527	0.441
9	1.082	1.00	0.906	0.836	0.775	0.726	0.679	0.642	0.602	0.536	0.450
10	1.080	1.00	0.908	0.840	0.781	0.733	0.687	0.650	0.610	0.545	0.460
12	1.076	1.00	0.915	0.844	0.791	0.745	0.700	0.664	0.626	0.563	0.478
14	1.072	1.00	0.922	0.848	0.801	0.756	0.713	0.678	0.642	0.582	0.496
15	1.070	1.00	0.925	0.860	0.808	0.763	0.720	0.685	0.650	0.590	0.505
18	1.064	1.00	0.935	0.876	0.825	0.781	0.740	0.706	0.690	0.617	0.532

$r_0 = 1$, $b_{70,300} = 1.047$, $a_{0,300} = 1.105$, $f_{0,1.2} = 0.548$

$$R = \frac{50^2}{(70+0)^2} \times 1 \times 1.047 \times 1.105 \times 0.548 = 0.324$$

whence percentage radiation at 8 cm. $= \frac{0.181}{0.324} = 56.3$ per cent.

We may discuss now the limit of applicability of the equation given above. In the first place its derivation is entirely empirical, there being no theory involved. It is a direct consequence of the four generalizations we developed from our experimental data, and therefore is subject to the same limitations. The tables we give for the values of the factors in the equation go only slightly beyond our experimental range, so that the extrapolation thus made cannot introduce large errors. Within the ranges for the different factors covered in our experiments the error is very small. This however, applies only to our machine under the conditions in which we use it. Since this is a typical American machine, and we have seen that the 10 cm. depth doses for several different machines of this type agree quite well, we may conclude that the equation with the factors we give may be used by others with a considerable degree of accuracy. Percentage values for other American machines[1] calculated by means of the equation and the factors given, probably would not vary from measured value by more than 5 per cent plus or minus. The measurements, of course, would have to be made with an instrument similar to ours.

The factor which varies a good deal with the machine, the tube and the radiologist (according to his idea of an erythema) is the milliampere-minutes required to produce a skin erythema under our standard conditions. It is very important to note that this *is not involved in the equation*. The values given by the equation are all in terms of a skin dose administered under the following conditions: Voltage 200 kv. (crest value), target-skin distance 50 cm., field 100 sq. cm., filter 0.5 mm. Cu. (A thin aluminum filter should also be used to remove the soft secondary radiation of the copper filter.) Each radiologist must determine for himself the milliampere-minutes required to produce an erythema under these conditions. Having done that, however, the equation will give him not only the depth doses, but also the milliampere-minutes for any other distance, filter and size of field. An example will make this clear. For our machine, 320 milliampere-minutes are required to produce a mild erythema on the average patient, under the conditions adopted as standard for the equation. Accordingly in our case our unit skin dose requires 320 milliampere-minutes. The equation enables us to calculate the surface radiation under different conditions in terms of this unit. The milliampere-minutes will be inversely proportional to the amount of radiation effective at the surface as calculated. Thus for a 70 cm. distance, a field of 150 sq. cm. and a filter of 1 mm. Cu., the surface radiation is

$$R = \frac{50^2}{(70+0)^2} \times 1 \times 1.061 \times 1.04 \times 0.635 = 0.356$$

$$\text{Therefore milliampere-minutes} = \frac{1}{0.356} \times 320 = 900.$$

This value for the milliampere-minutes applies only to our machine, since it is based on 320 ma.-min. for the standard dose. The ratio $\frac{1}{0.356}$ however, is probably applicable to other machines of the same type for the change in distance, filter and area here considered. For any other set of conditions it can be calculated in a similar manner. We are unable to compare directly our ratios for the different filters with those obtained for other machines, because there is practically nothing in the literature on this subject. We cannot say, therefore, just what error might be introduced in transferring our data for the filtration factors to other machines for purposes of skin dosage. The skin area factors (a_{zA}) and the beam area factors (b_{xA}), however, can be used for all machines without appreciable error.

A radiologist may make an indirect comparison of the radiation produced by his machine with the radiation which we used in our experiments by determining the "effective" wave-length according to

[1] It is safest not to assume that the equation applies to machines of the Rieber design or continuous current machines.

Duane's methods.[1] We have determined the effective wave-length using three different ionization chambers, and the results are shown in Table XVIII.

TABLE XVIII

A	B	C	D	E	F	G	H	K
Cu. Thick. in mm.	Small Bakelite Chamber				Large Chamber Silk Plates		Large Chamber All Alumimum Plates	
	In Air		On Water					
	Per Cent Transmitted	Eff. Wave Length A. U.	Per Cent Transmitted	Eff. Wave Length A. U.	Per Cent Transmitted	Eff. Wave Length A. U.	Per Cent Transmitted	Eff. Wave Length A. U.
0	545	.....	458	.....	329	.....	390	
0.2	201	.....	183	.....	176	.....	190	
0.4	117	.....	116.8	.....	114	.....	118	
0.5	100	0.152	100	0.156	100	0.155	100	0.168
0.7	81.4	.....	81.1	.....	82.2	.....	77.3	
0.75	78.7	0.150	77.8	0.150	79.2	0.149	73.3	0.158
1.0	65.2	.....	64.5	.....	66.7	.....	59.7	
1.2	58.1	.....	56.7	.....	58.3	.....	49.6	
1.5	47.8	.....	45.6	.....	46.7	.....	39.5	
1.7	41.6	.....	40.0	.....	41.1	.....	35.0	
1.75	39.3	.....	38.4	.....	40.3	.....	32.7	

The figures in Columns B and D were obtained with the small bakelite chamber; those in Columns H and F with large ionization chambers having plates of aluminum and silk ribbon, respectively. It will be seen that all the values of the effective wave-length (for radiation transmitted through 0.5 and 0.75 mm. Cu.) agree except those obtained with the "aluminum" ionization chamber (the aluminum plates of this chamber make up a total thickness of one millimeter). It is to be noted that the values given in the Column B were obtained with the chamber in air while the values of Column D were obtained with the chamber half submerged in the water phantom. They are averages of a large number of determinations made at different distances from the Coolidge tube and with different diaphragms. These represent most closely the radiation which is effective on the surface. Duane[1] states that for a voltage of 200 kv. (crest value) the effective wave-length for radiation filtered by 0.5 mm. Cu. is in the neighborhood of 0.16 A. U. Glasser[1] gives 0.15 A. U. as the effective wave-length for the above voltage, and 0.75 mm. Cu. This is in good agreement with our values. Both Duane and Glasser used different machines from ours. We can be fairly sure, therefore, that our values for the filtration factors can be applied to other machines without introducing a large error.

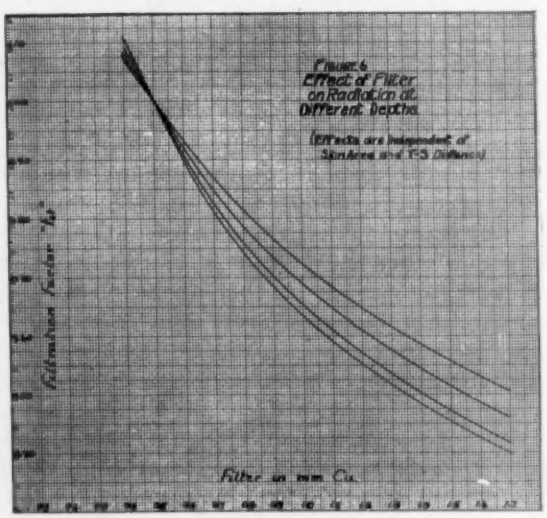

FIG. 6.

[1] DUANE, W. Am. J. ROENTGENOL., Dec., 1922, ix, 781.

[1] GLASSER, O. Am. J. ROENTGENOL., May, 1923, x, 405.

Before leaving this subject we wish to point out the simplicity of using the equation. In the first place very little thinking is required. The radiologist simply writes down the data of the problem as shown below:

$$R = \frac{50^2}{(X+Z)^2} r_Z b_{XA} a_{ZA} f_{Zt}$$

Target-skin distance $X = 60$ cm. (for instance)
Tissue depth $Z = 10$ cm.
Thickness of Cu. filter $t = 0.8$ mm.
Area of field $A = 200$ sq. cm.

Then he writes down the symbols for the factors with the proper subscripts, thus:

$r_Z = r_{10}$ $(Z = 10)$
$b_{XA} = b_{60,200}$ $(X = 60, A = 200)$
$a_{ZA} = a_{10,200}$ $(Z = 10, A = 200)$
$f_{Zt} = f_{10,0.8}$ $(Z = 10, t = 0.8)$

He is now ready to look up the proper values for these constants from the tables given. Thus in Table XV, for $z = 10$ he finds 0.467 for the value of r_{10}. Therefore he sets down[1] $r_z = r_{10} = 0.467$. Similarly he looks up the value of $b_{60,200}$ in Table XIII. The desired value is found in the line for $X = 60$ and the column for $A = 200$. It is 1.030. Therefore $b_{XA} = b_{60,200} = 1.030$. In Table XVI he finds the value for $a_{10,200}$ at the intersection of the line for $z = 10$ and the column for $A = 200$. Hence $a_{ZA} = a_{10,200} = 1.20$.

In a similar manner he finds the value of $f_{10,\ 0.8}$ in Table XVII at the intersection of the line for $Z = 10$ and $t = 0.8$.

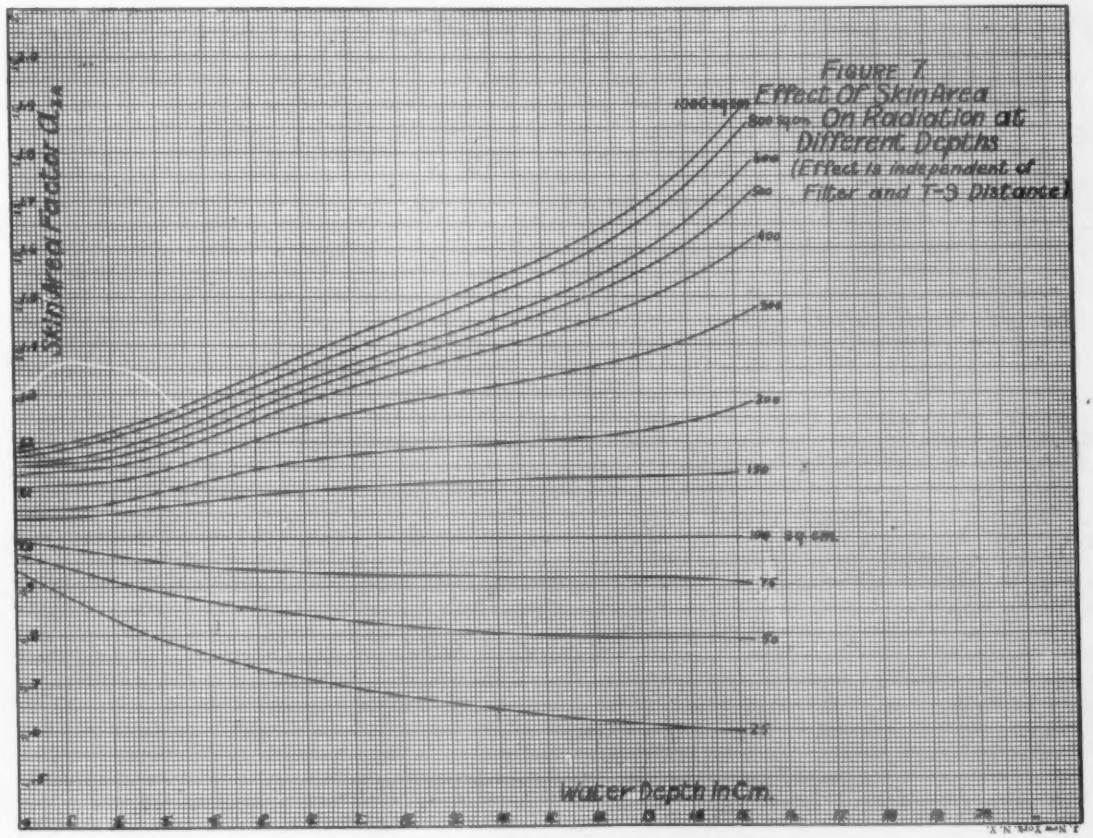

FIG. 7.

That is $f_{Zt} = f_{10,\ 0.8} = 0.781$.

Substituting these values into the equation he finds the amount of radiation for these conditions in terms of the unit adopted here.

$$R = \frac{50^2}{(60 + 10)^2} \times 0.478 \times 1.030 \times 1.20 \times 0.781 = 0.236$$

[1] In practice he would write the value next to the symbol in the above list. This, however, would cause confusion in this explanation.

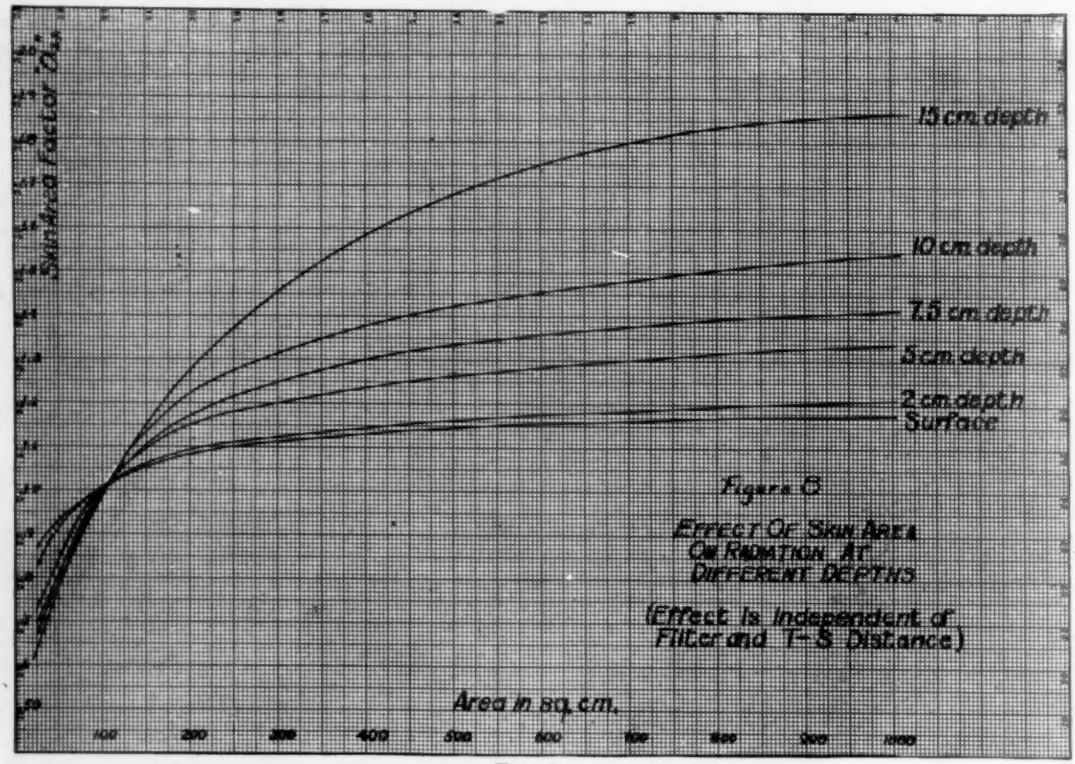
15 cm. depth
10 cm. depth
7.5 cm. depth
5 cm. depth
2 cm. depth
Surface
Figure 6.
Effect Of Skin Area On Radiation At Different Depths
(Effect Is Independent of Filter and T-S Distance)
Area in sq. cm.

FIG. 8.

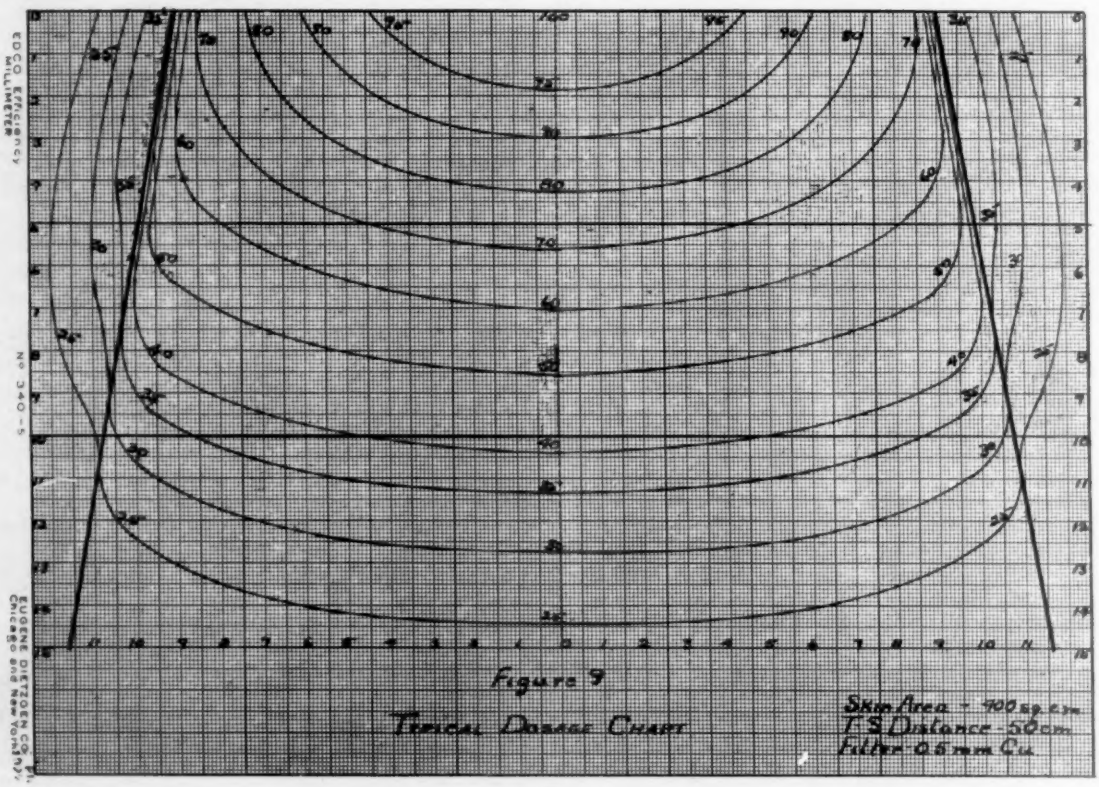
Figure 9
Typical Dosage Chart
Skin Area - 400 sq. cm.
T.S. Distance - 50 cm.
Filter - 0.5 mm Cu.

FIG. 9.

(Using the slide rule the above calculation can be made in less than one minute.)

To determine the depth dose in *percentage of the skin dose for the same conditions* it is necessary to calculate the surface radiation. Some of the factors will be the same as in the previous determination, but it is best for the radiologist to look up all of them and list them in the manner shown above as if this was an entirely new problem. For the sake of brevity we do not do this here.

$$R_{surface} = \frac{50^2}{(60+0)^2} \times 1 \times 1.030 \times 1.06 \times 0.74 = 0.561$$

Therefore the percentage dose $= \frac{0.236}{0.561} =$ 42.1 per cent for the conditions of this problem.

The use of this equation is practically a mechanical process. The only thing that the radiologist must remember is that the results are always given in terms of the surface radiation delivered under the standard conditions of the 50 cm. target-skin distance, 100 sq. cm. field, 0.5 mm. Cu. filter, the voltage being 200 kv. (crest value). (By substituting in the equation the value of the different factors for these conditions it will be seen that $R = \frac{50^2}{(50+0)^2} \times 1 \times 1 \times 1 \times 1 \times 1 =$ 1.)

The four tables given in this paper for the factors involved in the equation enable us to calculate values of R for over 30,000,000 combinations of distance, area of field, filter and tissue depth. Values for the factors intermediate to those given, however, might be desired in practice. For this purpose we have worked out the curves shown in Figures 3, 6, 7 and 8. It is perhaps superfluous to explain the use of these charts.

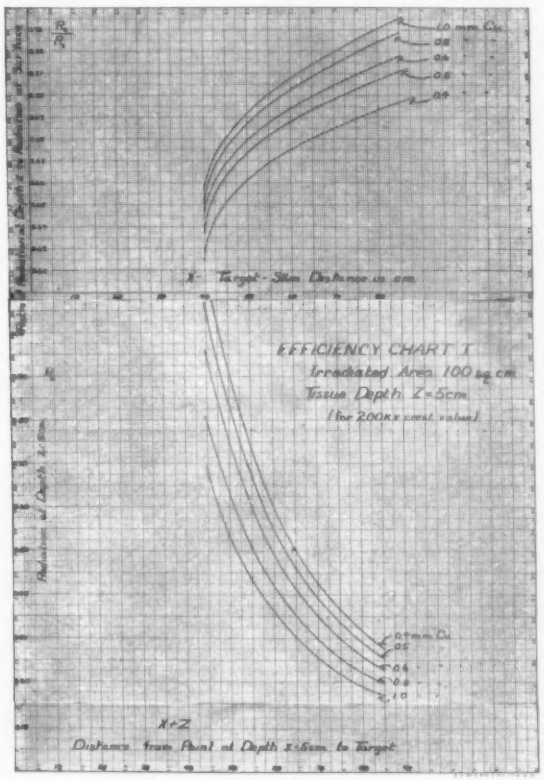
EFFICIENCY CHART I
Irradiated Area 100 sq cm
Tissue Depth Z=5cm
(for 200 K.V. crest value)
X= Target-Skin Distance in cm
X+Z
Distance from Point at Depth Z=5cm to Target

CHART I.

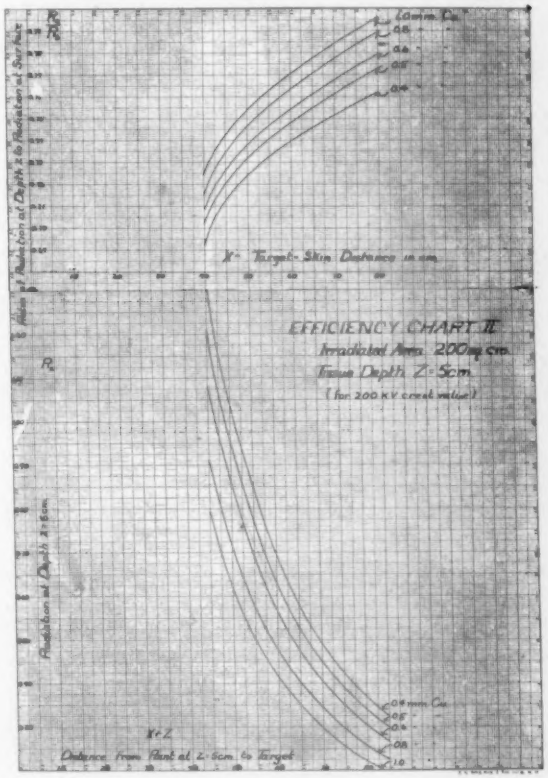
EFFICIENCY CHART II
Irradiated Area 200 sq cm
Tissue Depth Z=5cm
(for 200 K.V. crest value)
X= Target-Skin Distance in cm
X+Z
Distance from Point at Z=5cm to Target

CHART II.

EFFICIENCY CHARTS

The data we have presented so far offer a method of comparing the amount of

radiation available at any tissue depth under different conditions of treatment. The information we may derive from such comparisons is quantitative. For instance, if we compare two treatments given under the same conditions except for the size of the field, we can tell not only which one supplied the larger amount of radiation at a certain depth, but also *how much more* the radiation was. We shall make use of methods of choice reduce to two or a combination of these. Taking as a criterion the length of the treatment required to deliver the desired amount of radiation at a certain depth, it will readily be seen that there must be a happy combination of the different factors which will result in the shortest treatment for the given depth dose. To work out this problem we must know the depth dose, not only in

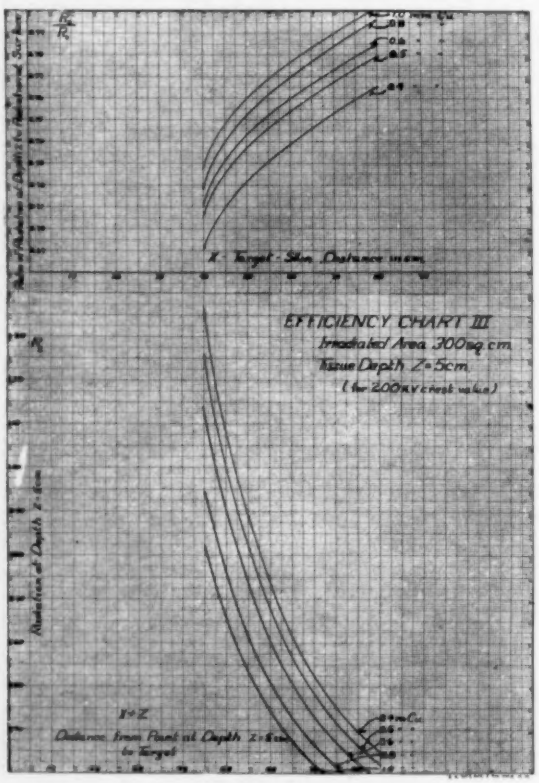
EFFICIENCY CHART III
Irradiated Area 300 sq cm.
Tissue Depth Z = 5cm.
(for 200 KV crest value)
X Target - Skin Distance in cm.
Radiation at Depth Z = 5cm.
X+Z
Distance from Point at Depth Z = 5cm. to Target

CHART III.

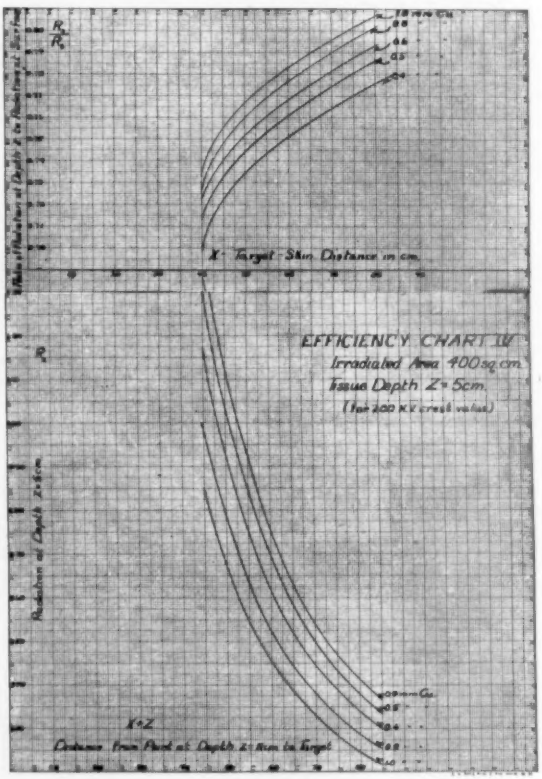
EFFICIENCY CHART IV
Irradiated Area 400 sq cm.
Tissue Depth Z = 5cm.
(for 200 KV crest value)
X Target - Skin Distance in cm.
Radiation at Depth Z = 5cm.
X+Z
Distance from Point at Depth Z = 5cm. to Target

CHART IV.

this fact now to determine the most efficient or economical way of delivering the desired amount of radiation at a given tissue depth.

We know that an increase in the area of the field, the thickness of the filter, or the target-skin distance separately, results in an increased depth dose, other conditions being the same. Therefore if we wish to vary the depth dose when the same skin dose is administered, we have three separate ways of doing so, or we may combine all three. In practice really, the size of the field in general is set by the requirements of the case we are treating. For any particular case, therefore, the percentage of the skin dose, but relative to a fixed standard. It was with this idea in mind that, for the equation given above, we adopted as a unit the surface radiation required to produce an erythema at 50 cm., with a field of 100 sq. cm. and a filter of 0.5 mm. Cu. (placed on the diaphragm at a distance of 40 cm. from the target). All other figures obtained thereby are in terms of this unit. It is hardly necessary to add that the results are independent of the unit.[1]

[1] If the distance between two points is expressed in feet, yards or miles it is immaterial to the man who is walking from one to the other. He will have to expend the same amount of energy in any case.

We have worked out a graphical method which enables us to determine the most efficient or economical conditions of treatment to deliver a certain dose of radiation at a given tissue depth. A number of such "efficiency" charts are included in this paper. For the sake of brevity we shall not describe the construction of these charts, but simply explain their use. Taking Chart VIII as a typical one we have: An irradiated skin area of 400 sq. cm. (field

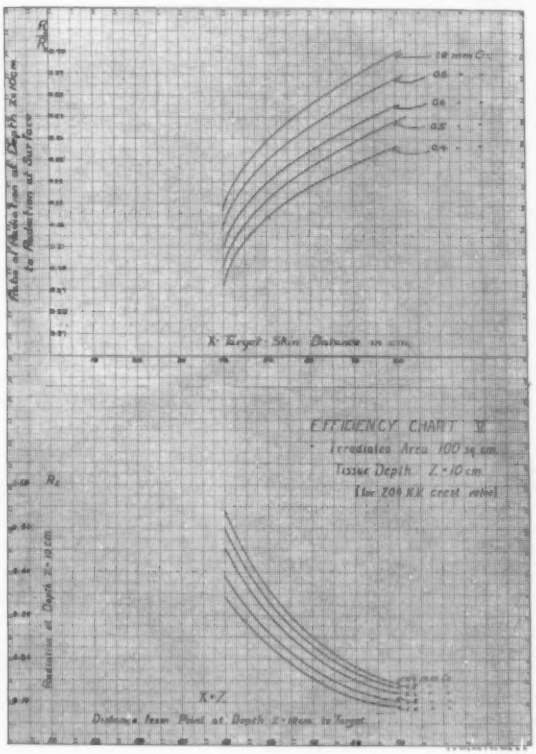
EFFICIENCY CHART V
Irradiated Area 100 sq. cm.
Tissue Depth Z=10 cm
X-Target-Skin Distance in cm.
X-Z
Distance from Point at Depth Z=10 cm. to Target

CHART V.

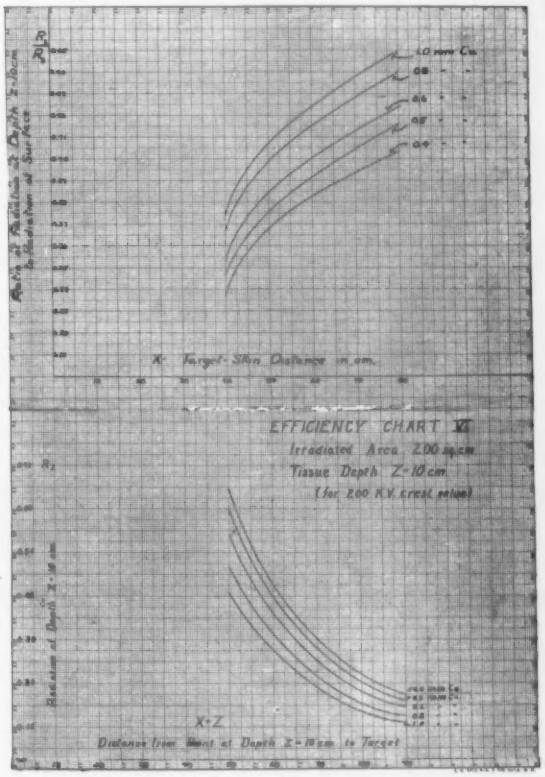
EFFICIENCY CHART VI
Irradiated Area 200 sq. cm.
Tissue Depth Z=10 cm
X-Target-Skin Distance in cm.
X-Z
Distance from Point at Depth Z=10 cm. to Target

CHART VI.

20 × 20 cm.) and a tissue depth of 10 cm. These conditions are set by the requirements of the case we wish to treat. We decide that the dose at a depth of 10 cm. shall be 80 per cent of a skin dose, and that it is to be administered through two opposite skin areas (400 sq. cm.). Accordingly for either area the dose at 10 cm. is 40 per cent or the ratio between depth radiation and skin radiation is $\frac{R_z}{R_s} = 0.40$. Going to the efficiency chart (VIII) now, we find on the scale for $\frac{R_z}{R_s}$ the point corresponding to a ratio of 0.40 and we draw a horizontal line A intersecting the curves M for the different filters. From the points of intersection we draw straight lines B to meet the corresponding curves N below; and from these we draw horizontal lines C to the scale for radiation at depth z = 10 cm. We are ready now to read the results. The lines B intersect the scale of target-skin distance at different points. These determine the distances which, coupled with the corresponding filters, will give a ratio of 0.40 between the surface radiation and the radiation at a depth z = 10 cm. Thus if a filter of 0.5 mm. Cu. is used, the target-skin distance must be 47.0 cm. to give the required percentage depth dose. Similarly for a filter of 0.6 mm. the required distance is 44.0 cm.; for 0.8 mm. it is 40.5 cm.; for 1 mm. it is 39.5 cm., etc. It will be noticed that the distance is shorter the thicker the filter, which is as it should be.

All these pairs of filter and distance fulfil the condition that the ratio $\frac{R_{z=10}}{R_s}$

= 0.40. Of these, however, only one is the most economical from the standpoint of the duration of treatment. We determine this in the following way: The intersections of the lines C and the scale of radiation at depth z = 10 cm. give us the values of the depth radiation corresponding to each set of filter and distance. The combination which gives the largest value for R_z is the most economical to use.

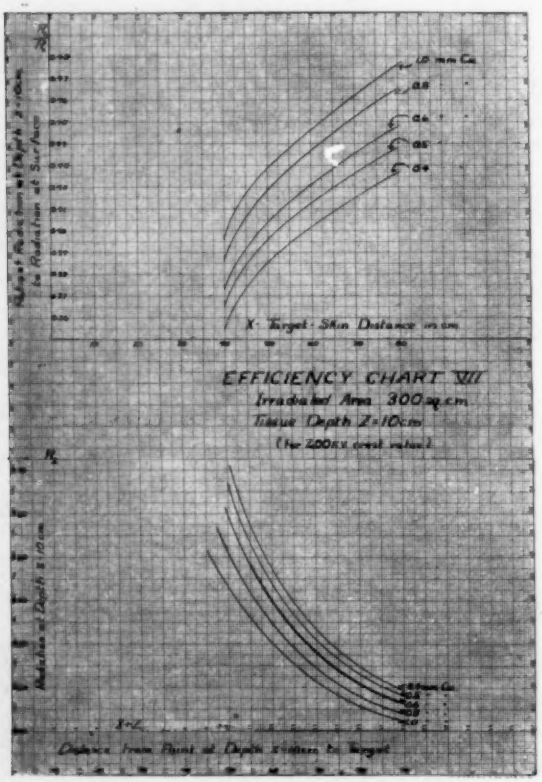
EFFICIENCY CHART VII
Irradiated Area 300 sq cm
Tissue Depth Z=10cm
(for 200 K.V. crest value)
X: Target-Skin Distance in cm
Distance from Point at Depth Z=10cm to Target

CHART VII.

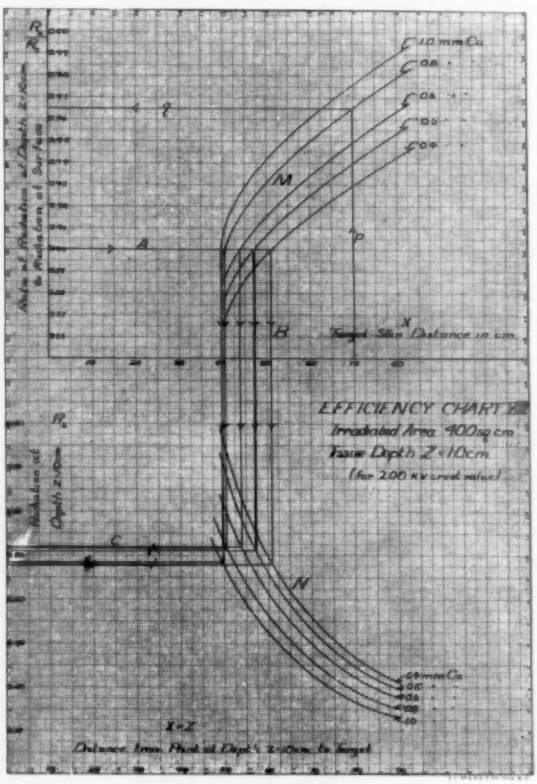
EFFICIENCY CHART VIII
Irradiated Area 900 sq cm
Tissue Depth Z=10cm
(for 200 K.V. crest value)
X
Target Skin Distance in cm
Distance from Point at Depth Z=10cm to Target

CHART VIII.

It will be seen at a glance from the chart that for this example the most economical combination is a filter of 0.6 mm. Cu. and a target-skin distance of 44.0 cm. Note that either a smaller filter or a larger one would be less economical in this case.

The next thing we wish to know is what milliampere-minutes to use to administer a skin dose under the conditions worked out for the chart; that is, 44.0 cm. distance, and 0.6 mm. Cu. We can do this by using the equation as already explained or more simply by means of the same chart. Thus the line C for 0.6 mm. Cu. intersects the scale for the radiation at depth z = 10 cm. at the point R_z = 0.52. This is the radiation at the 10 cm. depth in terms of our unit. Since the ratio between surface and depth radiation for this problem is 0.40, the surface radiation will be $\frac{0.52}{0.40}$ = 1.30 units. As already stated, with our machine it takes 320 ma.-min. to deliver the unit of radiation adopted. Hence in our case we would have to use $\frac{320}{1.30}$ = 246 ma.-min. to give a unit erythema dose under the new conditions. The value 320 ma.-min. varies from one clinic to another, but the factor 1.30 (or any other obtained from the chart) is applicable to practically all American machines without perceptible errors.

If we calculate the milliampere-minutes for each filter and distance which will give a ratio $\frac{R_z}{R_s}$ = 2.40, we can get an idea of the saving in time involved. This is shown in Table XIX.

TABLE XIX

Filter mm. Cu.	Distance cm.	R_z	R_s	Ma.-min. for our machine	Minutes	Per cent
0.4	51.0	0.486	1.22	262	68	111
0.5	47.0	0.512	1.28	250	62.5	102
0.6	44.0	0.520	1.30	246	61.5	100
0.8	40.6	0.516	1.29	248	62.0	101
1.0	39.5	0.480	1.20	267	67.2	109

It will be seen that for filters of 0.5, 0.6 and 0.8 mm. Cu., the time of treatment is practically the same. For a filter of 1.0 mm. Cu. the time is 9 per cent longer than for the most economical conditions; in practice the radiologist would probably use a 50 cm. target-skin distance. In that case the 1 mm. Cu. filter would necessitate a treatment of 436 ma.-min., or 44 per cent longer than the most economical one. The ratio $\frac{R_z}{R_s}$ in this case would be larger than before, but even if he adjusted the skin dose (giving less than an erythema dose) to get the same radiation at the 10 cm. depth, he would have to give a treatment of 396 ma.-min., or 16 per cent longer than the most economical one.

The above example illustrates the use of the charts for determining the most economical filter and distance in a simple case. In practice usually the requirements of the case are more complicated than we have assumed in the example. It is not necessary, however, to give more details since the method is the same. The use of dosage charts similar to Dessauer's to map out the treatment is to be recommended. Then for each port of entry our efficiency charts will determine the most economical filter and distance to be used. A typical dosage chart is appended to this paper.

The efficiency charts can be used for purposes other than the one outlined above. Thus the radiologist can determine at a glance what dose is possible to deliver at a certain depth with a given number of fields, or vice versa. For instance, taking

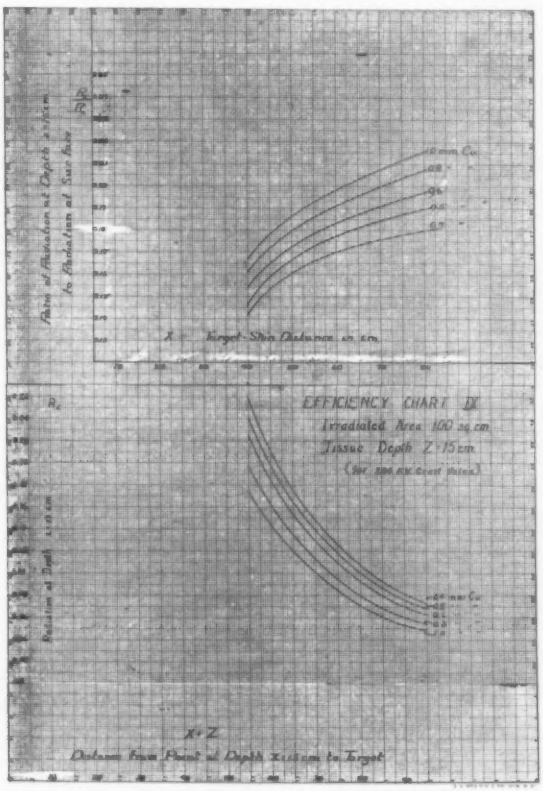

CHART IX.

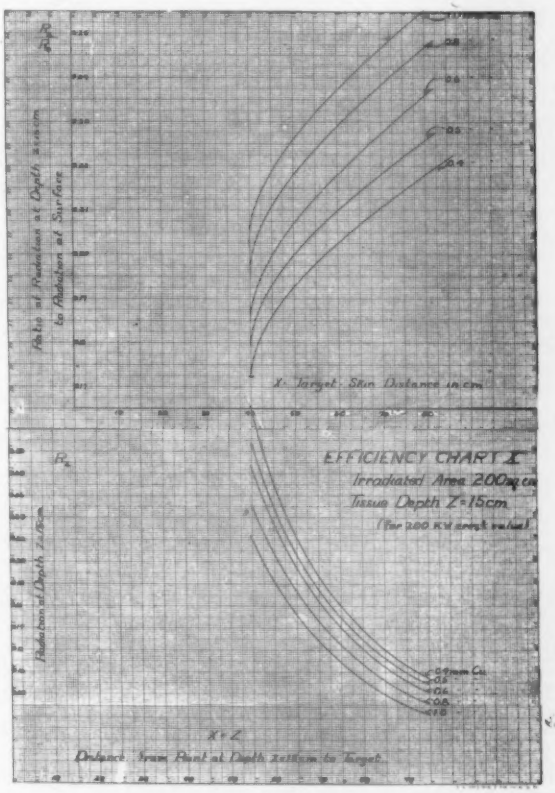

CHART X.

Chart IX he can tell immediately that with a field of 100 sq. cm., he cannot deliver one skin dose at 15 cm. by using four ports of entry (unless he uses a distance of perhaps 150 cm. and a thick filter, which is not practical). Chart X shows that if he uses fields of 200 sq. cm. he can do so. The larger fields are always more economical. Which one to use, however, must be decided on clinical ground alone.

Another use of the charts might be mentioned here. The percentage depth radiation at 10 cm. depth for those conditions is 46.8 per cent.

There is an important point we wish to mention concerning the results which we get either from the equation or from the charts. It will be remembered that the experimental work was done with a water-phantom $30 \times 35 \times 30$ cm. The results, therefore, are based on this volume of water as the absorbing and scattering medium. If in practice we use a smaller volume we cannot expect to apply these

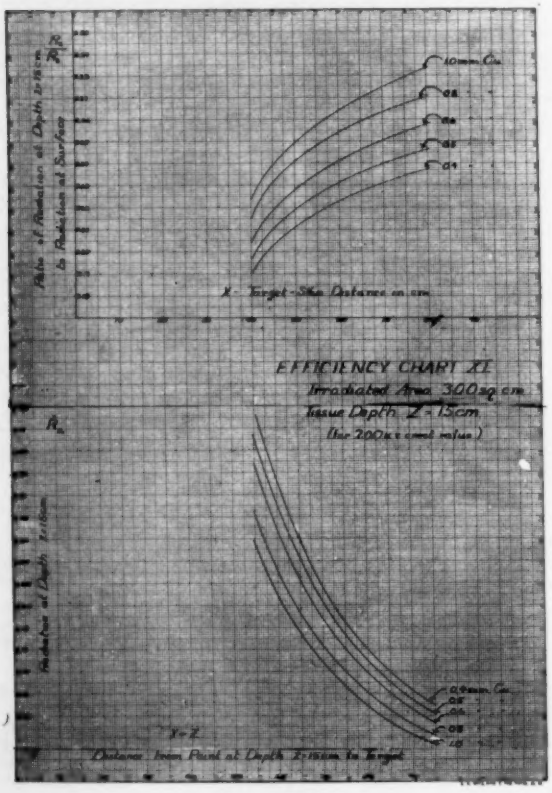
EFFICIENCY CHART XI
Irradiated Area 300 sq cm
Tissue Depth Z = 15cm
(for 200 K V crest volts)
X: Target-Skin Distance in cm
Y = Z
Distance from Point at Depth Z in cm to Target

CHART XI.

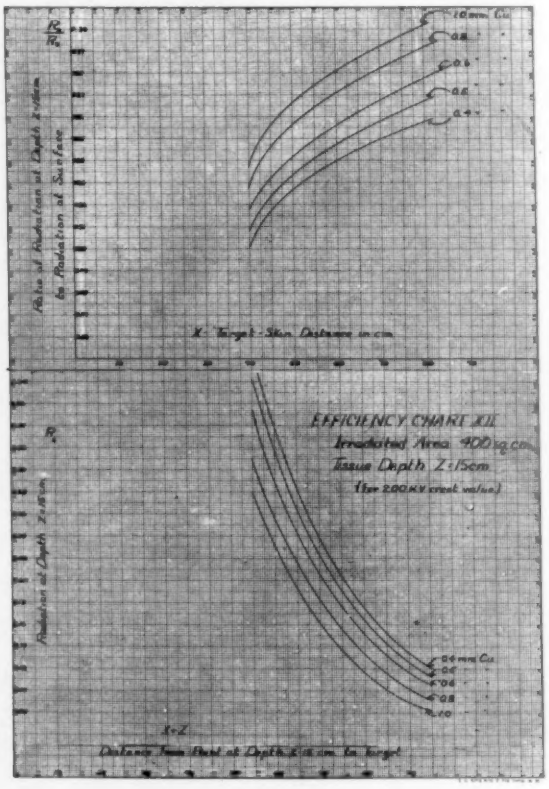
EFFICIENCY CHART XII
Irradiated Area 400 sq cm
Tissue Depth Z = 15cm
(for 200 K V crest volts)
X: Target-Skin Distance in cm
X = Z
Distance from Point at Depth Z in cm to Target

CHART XII.

radiation can be determined from the charts for the conditions of treatment which they cover. Thus, using Chart VIII we can find the percentage radiation at 10 cm. depth for a field of 400 sq. cm., a distance of 70 cm. and a filter of 0.8 mm. Cu., by drawing a line p from 70 on the target-skin distance scale to the curve for 0.8 mm. Cu. and thence a line q to the ratio scale. At the point of intersection we find $\frac{R_s}{R_z} = 0.468$. Hence the percentage

results without introducing a substantial error in extreme cases. For instance, in treating an arm, where the volume is small, the actual dose delivered at the center would be somewhat smaller than the data given in this paper would indicate. Radiologists have been using paraffin, beeswax, dough, water bags, etc. to increase the scattering medium in such cases and thus increase the depth dose. We recommend a similar procedure, for the additional reason that the conditions then will

approach more closely experimental conditions. For this purpose the volume should be built up to approximately the 30 × 35 ×30 cm. water-phantom. A convenient way of doing this is to have a frame into which the limb to be treated may be placed. Then the desired volume can be obtained by means of rubber bags containing water. The bulk of the volume may be built up with large bags and the intermediate spaces with rubber balloons only partly filled with water.

SUMMARY

1. The ionization experiments described in this paper were made with an ionization chamber fulfilling the requirements set forth by Friedrich.

2. Precautions were taken to avoid or correct for errors inherent in such measurements.

3. The data obtained led to the following generalizations which to our knowledge have not been made before.

A. The effect of the size of the field on the radiation effective at any particular tissue depth is the same for all filters and all distances used in practice.

B. The effect of the filter on radiation at any particular tissue depth is the same for all skin areas and all distances used in practice.

C. If all the dosage factors except the target-skin distance are the same, the relative depth doses depend only on the inverse square law.

D. For purposes of skin dosage in radiotherapy, the inverse square law is applicable, provided the same beam of radiation is effective at the different distances considered.

4. An empirical equation is developed for the calculation of the amount of radiation effective at any tissue depth (including the surface) under different conditions of treatment.

5. Tables and charts of the factors involved are given. They are for a voltage of 200 kv. (crest value) and a typical American machine.

6. From the data available in the literature it is shown that these factors can be used by radiologists using machines of this type without introducing a large error in the calculations.

7. "Efficiency charts" for a number of conditions of treatment are given. They enable the radiologist to determine the most economical filter and target-skin distance to use in giving any particular treatment.

8. The charts can be used also for other purposes, such as the determination of the percentage depth dose, the number of ports of entry to use in order to obtain the desired depth dose, etc.

9. Examples are worked out illustrating the use of the equation and the charts.

10. The limits of applicability of the generalizations, the equation and the charts are definitely set forth. The data given extend only slightly beyond the ranges used in the experiments, so that no large errors are introduced by the extrapolations. We believe that no error greater than 5 per cent plus or minus will result from the judicious use of our data by American radiologists.

11. Results are independent of milliampere-minutes.

STUDIES ON THE BIOLOGICAL EFFECTS OF X-RAYS*

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SCHENECTADY, NEW YORK

A SURVEY of the literature on the biological effects of *x*-rays shows that most investigators have used the methods of the histologist and the pathologist. It is clear, however, that disturbances which bring about directly observable changes in cells are usually of a rather gross nature and that the more delicate functions of cell parts cannot easily be investigated by such methods. In the investigations to be described a much more delicate method has been applied. The recent advances in the study of heredity have placed a new tool in the hands of the student of cellular physiology. With only a few exceptions the biologist has hitherto been limited to the observation of the reactions of the nucleus as a whole, and has had little or no opportunity to investigate the functions of its component parts.

Perhaps the most striking of the biological effects of *x*-rays is their effect on the chromatin of the nucleus. This chromatin forms the main constituent of the chromosomes. That the chromosomes determine at least some of the hereditary characters is now beyond doubt. Such hereditary characters provide a method of "labeling" a chromosome, and the behavior of such a character in heredity provides a certain indication of the functional activity of the corresponding chromosome. This new method has been applied to the study of the biological effects of *x*-rays. The experiments have been planned to show the physiological rather than the anatomical effects of the *x*-rays, and it is thought that the physiological effect is the primary one and offers the most delicate test of the reaction of the cell to *x*-rays. It is believed that the effects of *x*-rays on the chromosomes are of such a fundamental nature that they will be found to correspond throughout the animal kingdom, and therefore that the experimental animal may be chosen with reference only to its suitability for the experiments and without reference to its place in the animal kingdom.

When the investigations were first contemplated, a careful search was made for the most suitable biological material for *x*-ray experimentation. The fruit-fly, Drosophila melanogaster, was chosen. It is an animal the biology of which is well known. It is easily handled, can be conveniently bred in large numbers and has a short life-history. Its small size makes it particularly suitable for *x*-ray work, since for ordinary voltages (50,000 and over) all parts of its body receive approximately equal radiation.

The fruit flies are easily reared on fermenting banana jelly in small bottles. Starting in the egg, they pass through a larval stage lasting about five days. After this they become pupae and complete their metamorphosis into adult flies about ten days after the eggs from which they hatched were laid. The males are easily distinguished from the females, and by isolating pupae it is possible to mate the flies in pairs and thus to get exact counts of their offspring and to follow a given generation through its life-cycle.

The *x*-ray treatment was given with a Coolidge tube with tungsten target. In most cases this was water cooled. The voltage through the tube was always the same: 50,000. The *x*-rays were practically unfiltered, having to pass through only the glass of the *x*-ray tube, the air, and a single thickness of thin paper covering the small glass cups in which the flies were contained (Fig. 1) except when the flies were shielded from static electricity by placing them in a grounded lead box covered with aluminum three mills in thickness. In the latter case the *x*-rays had also to pass through the aluminum. The current passing through the *x*-ray tube varied with the experiment from a maximum of 50 ma. to a minimum of 1 ma. The distance likewise varied from 6.5 cm. to 70 cm. and the duration of the

* This is an abstract, and no references to the literature are here given. A complete list of the literature pertaining to the investigations is given in the detailed paper. The author of this paper was a warded third prize, $200.00, in the Leonard Prize contest.

exposure from three minutes to twenty hours and twenty minutes. Since the voltage was in every case the same, in specifying the dose it is only necessary to give the intensity and the duration. A dose corresponding to 1 ma. of current through the tube, received at a distance of 10 cm. from the target and lasting for one minute, was taken as a unit and represented by D. The number of the units, D, in any of the doses used is therefore represented by the formula:

$$\frac{\text{milliamperes} \times \text{exposure in minutes}}{(\text{focal distance in decimeters})^2}$$

The first investigation was a determination of the resistance of the fly to *x*-rays at the various stages of its life cycle. A

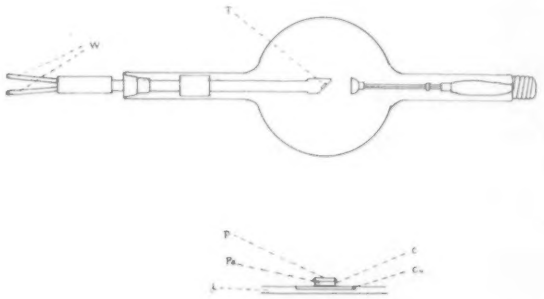

FIG. 1. Diagram of arrangement of apparatus used in the third series of *x*-ray experiments with drosophila.

dose which was just sufficient to kill 50 per cent of the animals at the end of five days was taken as the measure of the resistance. A more accurate result is obtained by taking the dose to kill 50 per cent rather than the dose to kill all, since in the case of all being killed the dose must be sufficient to kill the most resistant, and is therefore a measure of the resistance of that fly only, while in the case of 50 per cent being killed the dose represents approximately the average resistance.

The results of this investigation are represented in the graph (Fig. 2). In the case of the embryo, 50 per cent were killed in five days by a dose of 8 D (50 ma., 1 min., 25 cm.). The resistance gradually increases with age until during the latter half of the larval period a dose of 32 D is required to kill 50 per cent in five days. At the beginning of pupation there is a slight drop in the resistance followed by a sudden increase until at the time of emergence of the adult fly a dose of 630 D is required to kill 50 per cent in five days. It was necessary to obtain this data as a foundation for further work on the fruit fly. Incidentally the data show that the resistance of the fly increases with its metamorphosis and is very great in the adult fly. From this point of view the data provides another instance of the well-known theorem that actively growing and undifferentiated tissue is the most sensitive to radiation while tissue which has become stationary in its growth processes and fully

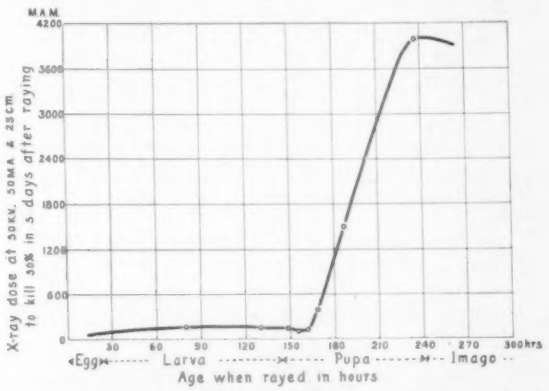

FIG. 2. Graph showing variation with age of resistance to *x*-ray in drosophila.

differentiated is the most resistant. Experiments were also made in which the flies were reared at different temperatures. When due allowance is made for the shorter or longer periods of development at those temperatures the effect is found to be the same for the same dose. By breeding the flies treated in the above experiments the sterilization dose was determined. It was found to be approximately 50 D for the female.

Since the experiments which follow deal with the effect of *x*-rays on the germ cells it will be well to review briefly what is known of the phenomena of reproduction in the fruit fly, filling in the gaps from our knowledge of the phenomena in other insects. The eggs are arranged in the ovaries in series (Fig. 3) there being about twenty such series in each ovary. In any one series the eggs nearest the oviduct are more nearly mature than those farther from it. At any one time there are from

twenty to forty eggs in the same stage of the maturation process. A somewhat similar condition occurs in the case of the testis. There the stages in the development of the spermatozoa are arranged in series in such a way that the more advanced stages occur nearest to the ducts.

The effect of radium rays on the testis of a locust has been investigated by Mohr and two of his illustrations are reproduced in Figure 4. This insect is especially favorable for the study of the germ cells. The figure shows very clearly that the radium

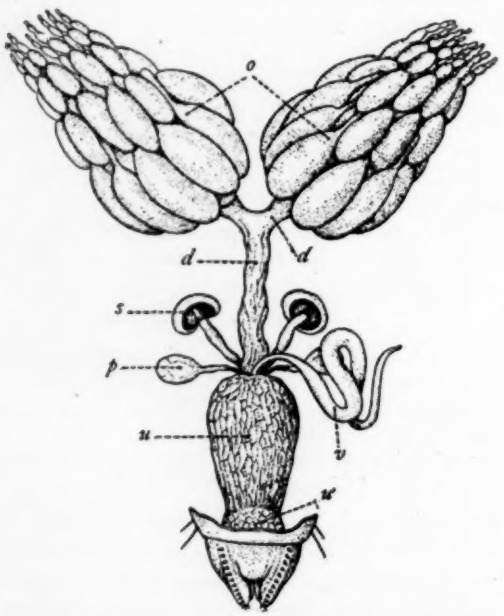

FIG. 3. Female generative organs of drosophila. d. oviducts; o. ovaries; s. spermathecae; u. uterus. After Nonidez.

rays affected only cells in certain stages of development. In the testis the primitive germ cells or spermatogonia continue to multiply throughout the life of the animal. The process of spermatogenesis by which spermatozoa are formed from the spermatogonia begins as the animal approaches maturity and continues during the rest of its life. In spermatogenesis, a period during which the spermatogonia, now called primary spermatocytes, enlarge in size and the chromosomes become associated in pairs, called the growth period, is followed by the maturation period in which there are two cell divisions. The chromosomes are small bodies of characteristic size and shape which occur in the nuclei of all the cells in the animal. The number, size and shape of the chromosomes in the nuclei of the body cells or primitive germ cells of any species of animal is constant and whenever such a cell divides the chromosomes divide. During the maturation divisions, however, the number of chromosomes in a cell becomes halved, owing to the fact that in the primary spermatocytes, referred to above, the chromosomes become associated in pairs and at the first maturation division the members of these pairs simply separate, one member going to each of the secondary spermatocytes which then contains the equivalent of only half the chromosomes of a body cell or primary germ cell. Since the chromosomes divide at the second maturation division the mature sperm have also half the chromosomes contained in the primitive germ cell.

Mohr's work on the locust and less clearly the work of other investigators on different animals, including mammals, shows that the stage in the development of the spermatozoa in the testis which is most susceptible to *x*-rays is the one referred to as the growth period during which the chromosomes become arranged in pairs previous to the first maturation division.

The processes by which a mature egg is formed from a primitive germ cell are exactly similar to those described as occurring in the development of the spermatozoa, there being a period of increase in size and pairing of the chromosomes followed by two maturation divisions during which the number of chromosomes in the cell is halved. The work of the writer on the fruit fly shows that in the case of the development of the egg, as in that of the sperm, the most sensitive stage is probably also the growth period during which the chromosomes are paired, although the period of the two maturation divisions is almost but not quite as sensitive. When virgin females of the fruit fly are treated with *x*-rays (50 ma., 3 min., 15 sec., 25 cm.) they produce a few offspring at the beginning of the normal reproductive period and then are sterile for a period (5 to 6 days) corresponding to the period elapsing

between the beginning of the growth period and the formation of the mature egg. The studies on crossing over to be described later show that the beginning of the growth period is probably the most sensitive stage in the ovary.

There is a considerable body of evidence to show that the chromosomes are particularly susceptible to *x*-rays. It becomes, therefore, of importance to discover just how they are affected and at what stage. The next series of experiments by the writer throws light on this question. In order to explain the method of experimentation it is necessary to add somewhat to the description already given of the development of the germ cells. In the male fruit fly it has been found that all the pairs (in this case four) of chromosomes in the body cells and primitive germ cells are not composed of equal partners, there being one pair in which they are markedly different (Fig. 5). These chromosomes are called the X and Y chromosomes. During the process of spermatogenesis these chromosomes become separated so that half of the spermatozoa contain one X chromosome and half one Y chromosome. In the female the case is different, the place of the Y chromosome being taken by an X chromosome so that there is a perfect pair in this sex and each mature egg contains one X chromosome. When an egg is fertilized by a sperm containing an X chromosome it develops into a female and when it is fertilized by a sperm containing

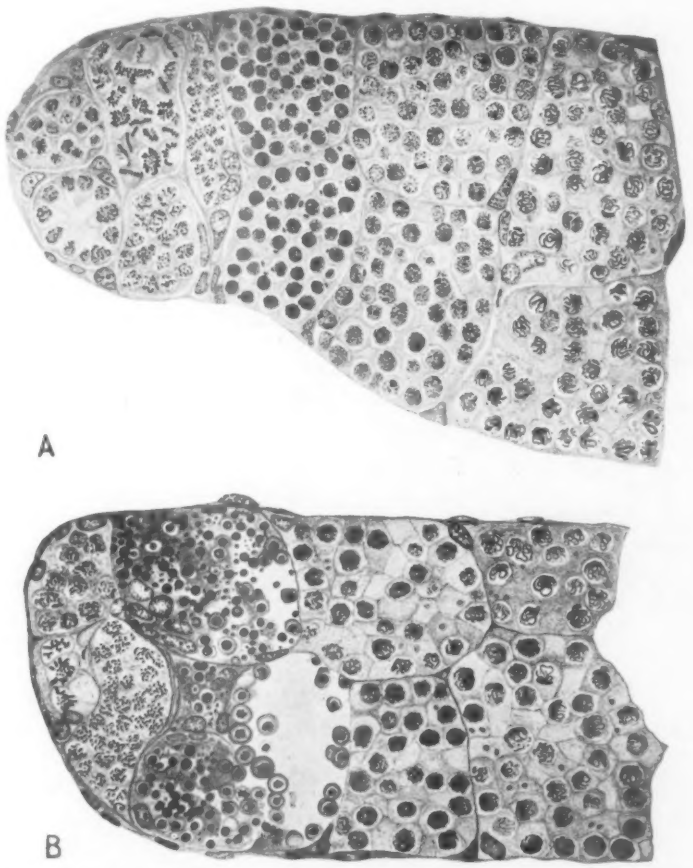

FIG. 4. Longitudinal sections through testes of Dectitus. A. normal testis from control; B. testis from individual treated with radium. Note that the region of the testis affected is that occupied by the early stages of the primary spermatocytes. The nuclei of these cells in the irradiated testis are represented by black bodies of irregular size and the cytoplasm is in some cases completely disintegrated. After Mohr.

a Y chromosome it develops into a male.

Through the extensive work on heredity in this species of fly it is possible to associate with the X chromosome certain definite and easily recognizable characters in the adult. It is therefore possible to treat the eggs of these flies (which is done by treating the entire adult female) with *x*-rays and by an examination of the flies which develop to determine the presence or absence of the X chromosome. Such was the plan of the experiments of the writer, and they have shown that *x*-rays when applied to the egg during the process of oogenesis may cause either the elimination of the X chromosome from the egg, in

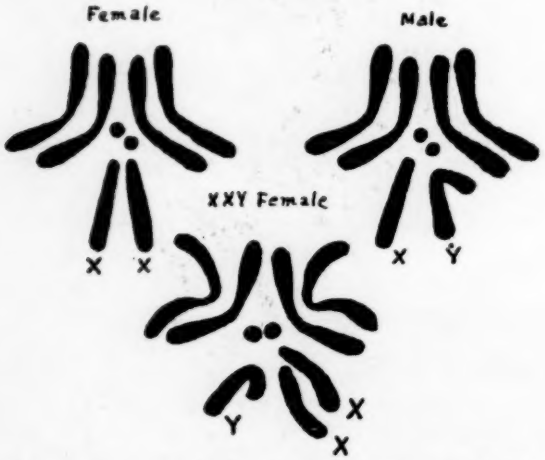

FIG. 5. Chromosomes of drosophila. Above and to the left those of the female including two X chromosomes, and to the right those of the male containing one X and one Y chromosome. Below XXY female showing the result of nondisjunction of the X chromosomes. After Bridges.

which case an egg without any X chromosome is formed, or the inclusion of two X chromosomes in one egg. When these eggs are fertilized they are viable and develop into exceptional offspring which may be recognized by their inherited characters. When an egg containing no X chromosome is fertilized by a sperm containing an X chromosome it develops into a male, while ordinarily an egg fertilized by a sperm containing an X chromosome gives rise to a female. When an egg containing two X chromosomes is fertilized by a sperm containing a Y chromosome it develops into a female, while ordinarily an egg fertilized by a sperm containing a Y chromosome gives rise to a male. Such females are exceptional in their inherited characters and in most cases are fertile and give rise themselves to exceptional offspring, so that the exceptional condition is inherited. The relation between the time at which the *x*-ray treatment was given and the time at

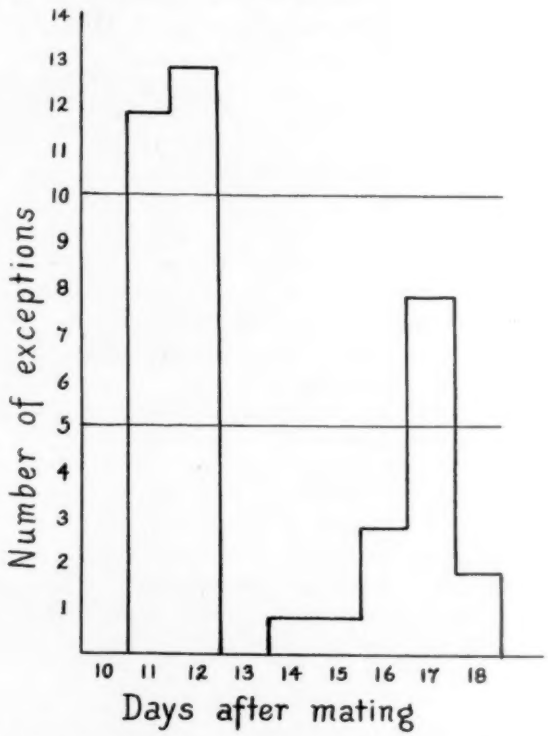

FIG. 6. Graph of time of emergence of exceptional sons of *x*-rayed females in third series of *x*-ray experiments with drosophila.

which the exceptional males and females were produced is of great interest. This is shown for the males in the graph (Fig. 6). It will be noticed that the exceptional flies are produced during one of two periods, either one to three days after the treatment or five to nine days after the treatment. It is possible that the first group of exceptional flies arose from eggs which were approaching the second maturation division and that those of the second group arose from eggs which were approaching the first maturation division at the time of the treatment. It is not necessary to assume a latent period in this action of the *x*-rays. Indeed it is improbable that any considerable time elapses between the time of *x*-ray treatment and the time at which the cell

becomes modified in such a way as to produce an abnormal distribution of the chromosmes.

One important result of the experiments is the demonstration that of all parts of the cell, the hereditary material responds most easily to the effects of *x*-ray treatment. This is made clear by the fact that the exceptional flies which develop from the *x*-rayed eggs are normal in every way except their hereditary behavior. It is possible that we see here the nearest approach to a specific effect of *x*-rays yet discovered since no other physical or chemical agent which produces this effect is at present known. The series of experiments shows that there is in the effect of *x*-rays on the germ cells a very clear case of an external agent which modifies the mechan ism of inheritance in such a way that a permanent effect is produced which is transmitted through successive generations.

In another series of experiments a still more delicate method has been used to test the effect of *x*-rays on the chromosomes. It is found that in the female the chromosomes of any one pair may interchange the character determiners which they carry. Thus one chromosome of a pair (in this case an X chromosome) may be known to carry the determiners for eosin eye color and miniature wings, and the other chromosome of the pair the alternative normal characters corresponding to these, namely, red eye color and normal wings. These chromosomes may interchange characters so that one contains the determiners for eosin eye color and normal wings and the other the determiners for red eye color and miniature wings. Under natural conditions the frequency of this exchange is quite definite and the per cent of cases in which it occurs is called the crossover value of the characters concerned. The interchange in all probably occurs during the synapsis stage. It is believed to depend on some physical property of the chromosomes.

Experiments were devised to test the effect of *x*-rays on the crossover value both in the case of the X or sex chromosome and the second pair of chromosomes. In the case of the X chromosomes it was found that *x*-ray treatment decreases the amount of interchange or the crossover value, as it is called. In the particular case investigated the normal crossover value was 30 and after *x*-ray treatment was reduced to 10. The experiment was made of varying the duration of the dose while keeping the dose itself (intensity $\times$ time) constant. It was found that within a factor of 375 (3 min. 15 sec. and 20 hrs. 20 min.) no difference could be observed. Since the effect of the *x*-ray treatment on the interchange of the hereditary determiners was evident over a relatively long period (six days) and the interchange itself occupies a shorter time, the experiments show that the effect of the *x*-ray treatment is not directly on the process of interchange, but rather on the physical condition of the chromosomes or the surrounding protoplasm. There is a large body of evidence which goes to show that the hereditary determiners are arranged in the chromosomes in a linear series and that the interchange of these determiners between the chromosomes is due to the two chromosomes of a pair breaking at corresponding points and interchanging corresponding parts. It has been shown that temperature affects the amount of interchange (crossing over) in the second chromosome and that temperature does not affect the amount of interchange in the X chromosome. It is, therefore, probable that in the effect of *x*-rays on the interchange of hereditary determiners in the X chromosomes there is a specific effect of *x*-rays, since all other attempts to produce the same effect by using other physical and chemical agents have failed.

Experiments were also carried out on the effect of *x*-rays on the interchange of hereditary determiners located in the second pair of chromosomes. In this case the *x*-ray treatment was found to increase the amount of interchange. In one of the cases included in the experiments a normal crossover value of approximately 5 was increased by *x*-ray treatment to approximately 25. It was also found that the *x*-rays affect to a different extent the interchange in different parts of the second chromosome.

It should be emphasized that while certain theories regarding the mechanism of inheritance have been used to explain

the results of the *x*-ray experiments, the results themselves depend in no way on any assumptions regarding the mechanism of inheritance, but entirely on the statistical findings of experiments. The general results of the experiments may be summarized as follows:

1. A curve showing the variation of susceptibility to *x*-rays with age in the fruit fly, Drosophila, has been obtained. This curve shows a sudden decrease in susceptibility during the latter part of metamorphosis, that is, after the main structure of the adult fly has been laid down.

2. The sterilizing dose of *x*-rays is small compared to the lethal dose for the adult fly. A dose can be found which gives temporary sterilization. In this case the mature eggs are still fertile, the sterile period beginning after their deposition.

3. The experiments show that *x*-ray treatment affects the distribution of the chromosomes during the maturation of the egg, and that such eggs, although their structure has been altered by the *x*-rays, may nevertheless develop into adult flies and produce offspring.

4. The effect of the *x*-rays, consisting in an irregular distribution of the chromosomes, is inherited.

5. *X*-rays may cause a modification in the interchange of hereditary determiners between chromosomes. The effect of the same dose is not the same in each of the pairs of chromosomes nor in the different parts of any one pair of chromosomes. In the first or X chromosomes the amount of interchange is decreased, while in the second pair of chromosomes it is increased.

6. The effect of *x*-rays on the interchange of hereditary determiners is not directly on the process of interchange but on the chromosomes or the protoplasm surrounding them.

7. The duration of the *x*-ray treatment for the modification of the interchange of hereditary characters is immaterial provided the product, intensity $\times$ time, is kept constant.

8. Reasons are given for considering that certain of the effects of *x*-rays on the mechanism of inheritance are specific.

It is perhaps premature to discuss the bearing of these results on the practical use of *x*-rays. Certain points may, however, be noted. The experiments show that *x*-rays provide the first really practical and universally applicable method of modifying inheritance. In this respect *x*-rays will probably prove of great value in the study of heredity, and this study will in turn throw further light on the biological effects of *x*-rays. Whether *x*-rays will ever be applied to modify inheritance for practical purposes, for example, in agriculture, is a question.

It is known that the mechanism of inheritance in man is, at least in its main outlines, identical with that which occurs in the fly and other animals. The behavior of the chromosomes is the same and there is an uneven pair. Hereditary characters, such as color-blindness and hemophilia, behave in a manner precisely similar to the characters located in the X chromosomes of the fruit fly. The results, therefore, so far as they go, are directly applicable to the human subject. It is of course highly improbable that *x*-rays will ever be used intentionally to modify human inheritance. However, with the present use of *x*-rays both therapeutically and for the production of temporary sterilization it is not unlikely that modifications may be produced, especially as we already know of a number of cases of children born of mothers whose generative organs had received *x*-ray treatment.

It is believed, however, that it is not in the field of heredity that these results will be found to be of the greatest significance. The methods used in these experiments to test for biological effects of *x*-rays are undoubtedly much more delicate and far-reaching than any hitherto applied. These methods provide a means of analyzing the effects of *x*-rays on cells. They show how *x*-rays may produce a permanent change in a cell without altering its vitality. A method of experimentation has been developed indicating lines of further investigation which may help toward a clear understanding of the exact physical and chemical changes produced by *x*-rays in living protoplasm.

THE OCCURRENCE OF TWO HERITABLE TYPES OF ABNORMALITY AMONG THE DESCENDANTS OF X-RAYED MICE*

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INTRODUCTORY

FOR years attempts have been made to modify the germ plasm of a living organism. Various agents have been employed, many chemical, many purely physical. Among the latter, radioactive substances such as radium or mesothorium have been utilized. Roentgen rays have also been used. The object of this communication is to present a simple experiment in the application of *x*-rays to adult mice, together with a study of the appearance and inheritance of two peculiar types of abnormality among the descendants of the animals so treated.

The two types of abnormality described are striking, and, for the most part, unfavorable to the animals possessing them. The situation is therefore of interest, not only to students of heredity, but also to medical men interested in the theory or practice of roentgen-ray therapy.

It will be well to state at the outset that no far-reaching claim or assertion is made on the basis of the facts here presented. The situation is merely one of clear and characteristic new forms, and, occurring as they do in a mammal, they should, we feel, prove a source of speculation to all those to whom the great possibilities of the physical agents as modifying elements in biology or medicine have made their appeal.

Two main facts are of prime importance to any experiment with *x*-rays. These are the family and case histories of the individuals used, and the amount and nature of the radiation to which they were subjected.

History of Stock of Mice Used. For the benefit of the reader who has not followed in detail the development of genetics during the past two decades, it should be noted that mice are to be looked upon as, in a way, the pioneers among mammalian material used for experimental breeding. The hereditary behavior of more than one hundred color varieties is known and has been carefully recorded. Numerous investigators have for years been studying and placing on file data of the methods of inheritance of their morphological, physiological and psychological traits The result naturally is that *new* variations—new abnormalities—are clearly recognizable and can at once be compared with all known types in existence.

The race or stock used in this experiment was composed of brown mice, a race which for some years had been carried on as a fancy pen or strain of poultry would be, without the introduction of any new blood. They were therefore sufficiently inbred to have given ample opportunity for the cropping out of any latent defects of the types to be described. The failure of such abnormalities to appear in the stock either before treatment with *x*-rays or in the 2,000 control animals from the same stock while under close observation and study, forms strong evidence that the *x*-rays themselves were the agent that actually brought about the changes producing the abnormalities.

History of the Individuals Used. Four female and three male mice, all adults, were used in the experiment described. None of the females were pregnant at the time of exposure. The numbers (for identification) of the females were 83, 84, 85 and 86; and of the males, 36, 40 and 42. The mice were in good health at the time of exposure and remained so afterward. They did not, however, produce any young until more than ten weeks after radiation. This seems to indicate clearly

* The authors of this paper were awarded honorary mention in the Leonard Prize contest.

(1) that none of the young descended from them could have been in utero during the exposure (the gestation period being approximately twenty-one days) and (2) that the estrous cycle and process of ovulation was badly disturbed, or that it was normal but that several of the ovulations following exposure produced only dead or impotent eggs, or that the vaginal or uterine secretions were so altered by radiation that no sperm could survive long enough to reach the ova.

Unfortunately the males were not separately tested, and it is not possible, therefore, to say whether they were affected or not. Since the exposure, however, was dorsal and the testes were well protected from above by their ventral position, it seems much more likely that the ovaries were, of the two types of gonads, the more readily reached, and therefore the more easily modified.

Exposure. The dosage was of twelve seconds' duration on each of five successive days. The target skin distance was 12 in.; the milliamperage 10; the spark-gap 2½ in. No filter was used. The whole amounted to ⅕ of a human erythemal dose given over the whole dorsal surface of the animal on each of five successive days. Other groups of animals received heavier doses, but need not be described here. As before stated, the treated mice showed no ill effects other than the temporary slowing down of breeding already mentioned. Leaving now the account of the experimental animals, let us, before describing their descendants, examine very briefly the work done by other investigators while trying to modify the germ plasm with *x*-rays, or to test their direct effects.

HISTORICAL

Attempts to modify the germ plasm by the use of *x*-rays, radium, or other radioactive substances have been fairly frequent. The peculiar action of rays on protoplasm and their great possibilities as modifying agents of its normal processes are nowhere more clearly shown than by the series of experiments by Oscar, Guenther, and Paula Hertwig on the eggs and sperms of aquatic forms.

Among other things, they were able to demonstrate what amounted to a selective action of radium rays on the nucleus or nuclear material of the sperms and unfertilized eggs of frogs. When medium doses of radiation were used and the treated sex cell was fertilized by a normal untreated sex cell of the opposite sex, the resulting larva was deformed, abnormal and not particularly viable. When, however, a heavier dose was used, the nucleus of the sex cell was completely prevented from participating in cell division and development. An embryo was formed consisting of the nucleus of the untreated cell and the cytoplasm of both sex cells, such as it was. In these cases the embryos, which, as can be seen, were in a way pseudo-parthenogenetic, developed normally but were of a smaller size than the control embryos neither of whose ancestral sex cells had been treated by radiation.

This work does not prove the modification of the germ plasm within the soma to be possible. Neither does it attempt to test whether these abnormalities induced by the direct exposure of sex cells are inherited. It does, however, show that direct exposure of sex cells may result in modifying the nuclei of these cells in such a way as to produce abnormal individuals.

Fraenkel has reported on a small series of experiments with *x*-rays on guinea-pigs. He found that the effect of exposure differed in young and old animals. Thus, in adults there was a marked difference in the surface of the ovaries. That of the control was covered with protuberances, the Graafian follicles, while in the treated animals these had completely disappeared. By using pregnancy as a test, he was able to conclude that radiation of young animals slowed down the growth rate, but that in such animals pregnancy occurred proportionately much sooner after treatment than in the case of radiated adults. It is interesting to note in passing that none of the treated mice in our experiments produced young for at least ten weeks after treatment. They were adults of reproductive age when treated and the result parallels closely, therefore, that described by Fraenkel. The rays in his experiment were applied from the direction

of the head vertically through the body. The few young which were obtained from exposed animals were undersized. They also possessed bald spots in the same regions as those which became bald in the exposed animals themselves. He considers this to be a case of inheritance of an acquired character. As before stated, his numbers are too small to be conclusive, and *true* inheritance as such is not proven because he uses treated females, and the possibility of the transmission of a direct cytoplasmic change cannot be disregarded and is most certainly to be considered until eliminated.

In a paper reported at the Christmas meetings of the American Society of Zoologists at Boston (1922) Hanson describes the preliminary results of a series of experiments with *x*-rays on rats. For the most part, the effects which he describes are the result of direct radiation of animals in utero. In several animals so treated a few days before their birth, serious eye defects, hemorrhage of the brain, paralysis and sterility are among the results noted. It is interesting to note that Bagg found that both rats and mice treated with radium while in utero showed eye abnormalities and distinct nervous symptoms, tremors, and various degrees of ataxia.

Both these series of results suggest the interesting similarity between the conditions found in treatment in utero and those observed in certain of the descendants of *x*-rayed adult animals reported in this paper.

Two other experiments may be briefly cited as showing perhaps more clearly an upset of a definite sort in the internal organization of the sex cell. The first of these is the work done by Mavor on the fruit fly, Drosophila melanogaster. Here the cytology and genetic constitution of the types used have been well worked out. It has been clearly shown that a certain group of hereditary characters are either carried in or depend for their expression upon a particular chromosome. Mavor treated young female flies with *x*-rays and found in their offspring an unusually high proportion of cases involving abnormal distribution of the halves of a particular chromosome at maturation. The effect was that in many cases this chromosome failed to divide, with the result that the egg cell either had a double representation of the chromosome or else failed to receive it at all. The tendency to excessive abnormalities in the distribution of the chromosome in question was handed on for several generations.

Blakeslee and Gager working with the jimson weed, Datura stramonium, found a somewhat similar increase in the appearance of abnormalities in chromosome distribution following treatment with radium. They reported on this work at the Christmas meeting of the A. A. A. S., 1922. They had not carried the work far enough to determine whether the abnormalities so produced were going to be handed down to the descendants of the treated plants.

With these various facts in mind, it is not surprising that the use of physical agents should be suggested as a promising means of trying to reach into the germ cells and there upsetting the normal type of organization by a new one that is self-perpetuating by inheritance.

DESCRIPTION OF EYE ABNORMALITIES[1]

Drawings and photographs of animals showing this particular type of eye abnormality are shown in Figures 1 to 15 inclusive. In describing the abnormality it has been spoken of as one involving the eye alone. This, however, is far from being the case. A moment's consideration of Figures 9, 13, 14 and 15 will show clearly other regions that are definitely abnormal. Thus Figures 9, 13 and 14 show a fairly common expression of the abnormality. This type is acephalic and also extremely pale in color. Such animals are born dead. Usually by the time they are discovered in or near the nest, they have had all the brain or other material within the cranial cavity removed by their mother. In one case, however, we obtained such a young mouse so soon after birth that its mother did not have time to begin the process. This mouse had a clear lesion of the cranial region with a dried crusty scab on the surface. The cranial cavity seemed filled

[1] It is customary in genetics to give each inheritable character the heredity of which has been investigated, a letter by which to designate it. This letter is used in expressing its formula as regards mendelian inheritance. The letter is given here merely to make identification of the character easy in connection with other publications in which it may be used.

with fluid giving a rather marked hydrocephaly. It is undoubtedly true that the other mice of this "pale fetus" type had similar lesions.

Figure 15 shows another modification of the abnormality. In this case the upper jaw has been shortened and twisted upward producing a "bull-dog" mouse. Animals of this general type, but somewhat less extreme than the individual figured, have survived for a considerable period of time.

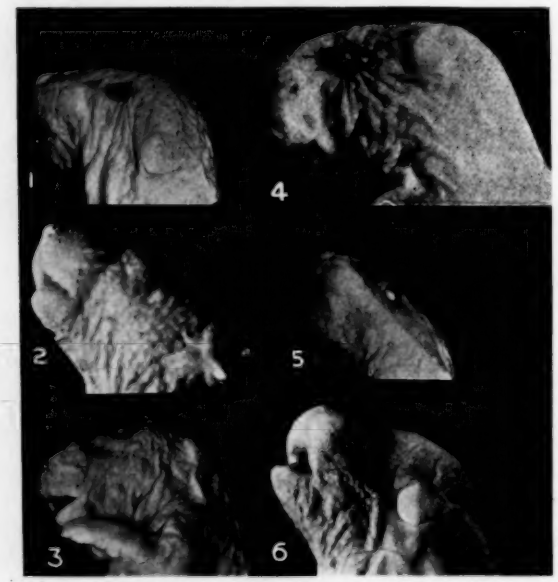

FIG. 1. Mouse 2068. A photograph of a day-old mouse preserved in 10 per cent formalin. The abnormal eye is clearly visible. It is a scabbed lesion of the type shown in Mouse 8597 (Fig. 13) except for the fact that the iris pigment and the lens do not show.

FIG. 2. Normal mouse showing the raised skin covering the eyeball with no sign of any external lesion.

FIG. 3. No. 2071. Clearly abnormal eye much like Mouse 9585 (Fig. 13). The lens appears as the light body surrounded by scabbed area and the iris pigment. The lesion covers the entire eyeball.

FIG. 4. Mouse 8621. FIG. 5. Mouse 2053. Typical pale fetuses of the same type as 9147 (Fig. 15). Note that in these cases, as in that, the entire cranial area, probably hydrocephalic in nature, has been removed by the mother mouse. The eyes are clearly dried and abnormal.

FIG. 6. Mouse 8670. A peculiar type in which the eye lesion is clear and in which the face is twisted and deformed, giving what may be called a "bull-dog" appearance. Several such mice have been recorded.

In such mice the teeth are not normally situated, being irregular in direction of growth as well as position.

Bagg, who has made a particular study of the structure of the brain of the abnormal-eyed mice, has in press a paper dealing

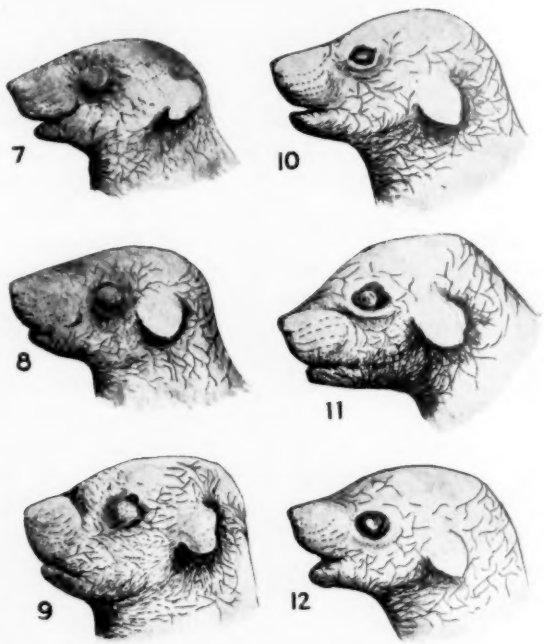

FIG. 7. 6591. Normal-eyed albino. Note that the skin over the eyeball is unbroken and smooth. There is no pigmentation visible. The eye is regular in shape and of normal size.

FIG. 8. 8550. Normal-eyed brown. Note that the appearance is very similar to 6591 (Fig. 7) but that the ring of iris pigment is slightly visible under the unbroken skin which covers the whole eyeball.

FIG. 9. 9490. Shows a very slight degree of abnormality. For the most part, the skin over the eyeball remains unbroken as in the foregoing examples. Just superior to the upper part of the eyeball there is a small lesion, dried and scabbed over with a crusted exudate, probably of non-inflammatory origin. Note the peculiar shortened foreface which this animal possesses. There is much variation in the length and type of foreface. The animal in question deviates much more from the normal type in this regard than in the eye lesion itself.

FIG. 10. 6589. A more clearly advanced case of a type of abnormality similar to 9490 (Fig. 9). Here the lesion is larger. The eye is more generally affected. It has become shrivelled and dried. In the center of the scabbed area is a crystalline structure, opaque and almost spherical. This is undoubtedly the lens, which, because of its durable nature, has not been modified fundamentally during the disarrangement of the rest of the eye.

FIG. 11. 7528. An abnormality of larger area, but less fundamental nature, than 6589 (Fig. 10). Here there is a large, irregular scabbed area, in which is situated the lens. Such an eye, as is the case with all these abnormals, is undoubtedly non-functional.

FIG. 12. 9585. An example of a much more extensive development of the abnormality. The whole eye is dried and laid bare by a lesion which removes the skin over the whole eyball. The iris pigment seems dried and condensed, giving a more concentrated appearance. The lens is present as in the other cases, lying on the surface, although somewhat imbedded in the dried, scabbed area surrounding it.

with this matter. It is, however, of interest to note, in passing, that in abnormal-eyed mice, degeneration has occurred in one or both of the optic nerves, and that other structural changes and abnormalities of a fundamental nature take place.

In the eye itself there are many degrees or grades of abnormality. An effort has been made to bring out in the figures some of the common types. In almost all abnormal-eyed young there is at birth a clear lesion in the region of the eye. These lesions vary in depth and extent. Rarely, instead of an actual external lesion, the eye presents a sunken and shrunken appearance. The eye is greatly reduced in size in such animals. As an animal of this type grows older the sunken eye either fails to increase in size or degenerates still further, producing a depression and, of course, complete blindness of the eye in question.

In eyes showing a lesion, degeneration of the eye elements themselves has proceeded to different degrees. Thus, in some cases, the eye is almost normal, with the exception that the lens is clouded or entirely opaque and there may be slight reduction in size of the eye as a whole. The eyes of some of the mice of this type present a marked degree of similarity to certain of the eyes obtained by Bagg after in-utero treatment of rats with radium.

Many other types are to be found. One with a minute scabbed lesion just above the eye is shown in Figure 3. More extensive lesions are shown in Figures 4, 5, 6, 7 and 8 in Figures 10, 12 and 15. In each of these cases a brief description of the conditions found has been placed in the explanatory notes to the figures.

Normal Overlaps. At birth the young obtained from abnormal × abnormal matings may have the following eye conditions, in so far as superficial external appearance is concerned:

1. Both eyes clearly abnormal.
2. Both eyes slightly abnormal.
3. One eye clearly, one eye slightly abnormal.
4. One eye clearly abnormal, one eye normal.
5. One eye slightly abnormal, one eye normal.
6. Both eyes normal.

When one eye only is abnormal it may be either right or left, with apparent equal frequency. The whole situation, therefore, suggests that two variables are involved: 1. The degree to which any eye is abnormal. This runs through a graded series from a condition in which there is a clear lesion with the entire eye dried and reduced, to a condition where no external lesion or reduction is observable, the eye apparently being normal. 2. The distribution of the abnormality to both, or to one, or to neither eye, in so far as external appearances are concerned.

FIG. 13. 8597. An interesting modification of the abnormality. The scabbed area is large and irregular and the lens small and out of normal position, being at the lower margin of the lesion. The iris pigment seems to be in the form of a clump of a symmetrical outline at the posterior margin of the lesion. Such a type as this shows a marked disarrangement of the eye.

FIG. 14. 8464. One of the more extreme manifestations of the abnormality. The lesion is deep, and, with the exception of a small lens near the center of the lower border, filled with a pigmented scab, probably representing a combination of the iris pigment and exudate.

FIG. 15. 9147. A very typical expression of the abnormality. This has been described as "acraniate-pale fetus." The whole animal is abnormally white and bloodless. The eyes are grossly abnormal, with a deep lesion and with the lens and ring of iris pigment exposed. When found, such embryos are almost universally without a top to the skull. This defect is undoubtedly primarily due to a lesion located there, although, except in rare cases, removal of tissue in this part by the parent renders exact description of the lesion in its original form impossible. These pale fetuses are always born dead.

Variation in inheritable characters is, of course, general. It is quite common to find that in the case of morphological characters this variation leads in the direction of the normal type to a point where it is by gross examination indistinguishable from the normal itself. Examples of this type of character have been recorded by Castle (1906) in the case of polydactylism in guinea-pigs; by Wright (1916) in the rough coated character of guinea-pigs, and in several characters in birds, notably feathered legs in pigeons; by Doncaster (1912) in web feet in pigeons; by Staples Brown (1908) in syndactylism and polydactylism; and by Davenport (1906) in rumplessness in fowls.

No extensive attempt has yet been made to determine what rôle modifying genetic factors are playing in the variations of the abnormal eye character in the material under observation. It is quite possible that one or more such modifying factors may be involved, and although their isolation and identification would be difficult, it should, and when opportunity affords, will be, attempted. A certain amount of the variation will, however, in all probability, be due to internal environmental influences—the shifting balance between organs, tissues and cells during ontogeny. This must remain as a source of uncertainty until our knowledge has advanced to a point sufficient to enable us to analyze and measure processes of this sort.

At present it will suffice merely to state that the fact that normal overlaps occur is not surprising, and that no new principle in this regard is involved in the case under consideration.

The eye abnormality first appeared in a brown male mouse, No. 1369. This animal was a grandson of two animals that had been exposed to *x*-rays. His parents had not been treated. One of his eyes was distinctly abnormal and degenerate to a point of failing to function.

In a subsequent litter from the same parents a brown female, No. 1373, also abnormal in one eye, was obtained. When these two animals were bred together evidence at once began to accumulate to indicate that the eye abnormality was a recessive character. From results later procured it became apparent that Male 1369 also carried the potentiality of giving progeny with abnormal feet. A more detailed treatment of the inheritance of these abnormalities will be found in a later section.

Although breeding experiments within the family in which the eye abnormality appeared were continued, they cannot afford as good evidence of the type of inheritance involved as can an outcross with a known but unrelated stock.

TEST OF INHERITANCE

There is a simple and effective test of inheritance which is made by crossing an abnormal-eyed (hh) male with an *unrelated*, normal-eyed female (HH), and then, by inbreeding their normal (Hh) F_1 generation descendants, produce F_2 and F_3 generation hybrids. Abnormal-eyed animals of these and subsequent generations should then be bred inter se and should breed like the original abnormals.

A test of this type was made by crossing abnormal-eyed Male 1369 with females of unrelated (Bagg's albino) race. The first hybrid generation (F_1) was normal-eyed. F_2 produced by crossing F_1 inter se, and further similar crosses gave a total of 113 normals and 29 abnormals. These abnormals and those of later hybrid generations bred together gave 16 abnormal in both eyes, 116 abnormal in one eye, and 36 normal (overlaps). Those of the 36 normal overlaps that were tested by breeding gave a result similar to those which were obtained in the *x*-ray lines 85 and 86 before any outcross was made.

The test of inheritance given above insures transmission of the character in question through the sperm. The possibility of the egg cytoplasm as a carrier is eliminated by using normal-eyed females of an unrelated race as the female parents of the hybrids from which the eye abnormality was later recovered.

It is only by some such test as the above that we can surely eliminate the possibility that direct transmission rather than true inheritance is involved.

The figures given above show clearly three main facts:

1. The eye abnormality is inherited.

2. Its inheritance is essentially mendelian in behavior.

3. A certain number of animals genetically abnormal-eyed are somatically normal-eyed, so far as gross anatomy is concerned. The percentage of these in this particular cross is shown in the progeny of abnormal-eyed individuals crossed inter se. Here out of a total of 168 young, 36, or 21.4 per cent, were normal-eyed. It will be recalled that when animals carrying the abnormal eye as a recessive were crossed together, 113 normal and 29 abnormal were obtained. The expectation on a mendelian basis is 106.5 normal to 35.5 abnormal. There is observed a slight excess of normals and deficiency of abnormals. If, however, among the somatically normal, a certain number are genetically abnormal, we may make a correction, purely for the basis of comparison.[1] When this is done, the numbers are 107.5 ± normal, and 34.5 ± abnormal—very close to the 106.5 to 35.5 ratio expected.

When the results obtained in the inbred family in which the eye abnormality appeared are considered, a situation closely resembling the foregoing is observed.

In this family, almost all the matings have been of abnormal-eyed mice inter se. From such crosses, a total of 447 young has been obtained. Of these, 374 are clearly abnormal in one or both eyes, and 73, or 16.3 per cent are normal in appearance. Many of the latter have been tested by breeding, and in each case in which such a test has been made, have been found to behave genetically as abnormal. The percentage of these genetically abnormal mice that are somatically normal is then about 15.1. Crosses of normals carrying "abnormal," inter se have given 75 normal and 15 abnormal young. On a mendelian basis 67.5 normal and 22.5 abnormal are expected. If a correction to account for the difference between genetic and somatic "normals" is made, the numbers become 72.8:17.2.

[1] The correction can be made as follows. If among the progeny of abnormal-eyed mice crossed inter se, 16.3 per cent are normal in appearance, then for the 29 abnormal young observed there must have been formed a certain number of somatically normal, but genetically abnormal animals. The number of these cannot be exactly told. It can, however, be estimated by considering the 29 abnormal young observed as representing 83.7 per cent of the total abnormals formed. When this is done, the number left to be estimated as somatically normal and genetically abnormal is 5.5. These should, in our calculation, be subtracted from the *observed normals* and added to the observed abnormals.

In the cross of abnormal-eyed with normals carrying abnormal, where a 1:1 ratio of the two types (normal and abnormal) is expected, the observed numbers are 52 normal and 40 abnormal. The expectation is 46:46. When a correction is made, the numbers come out exactly 46±:46±.

In general then, we may conclude that the genetic behavior of this character is mendelian, and sufficiently regular to enable us to have a fair degree of definiteness in predicting its place and rate of occurrence.

THE INHERITANCE OF ABNORMAL LEGS AND FEET

In showing the nature and types of this abnormality, we are handicapped by the fact that photographic representations are not particularly satisfactory because of the minute size of the parts involved. The drawings are therefore submitted in the hope that at least a general impression may be obtained of the more common types of the abnormalities.

Figure 16 shows a foot of Mouse 6107 in which there is a discolored hemorrhagic lesion and a slight shortening of the digits. In all other respects the foot appears to be normal. It may therefore be taken as approximating the normal type and as representing a very slight degree of abnormality. The three other legs and feet of Mouse 6107 were normal.

Figure 17 goes almost to the opposite extreme and shows the three abnormal legs of mouse 6047. In these the abnormality is marked. In the left hind foot the digits are absent as separate units, the only possible indication or trace of them being slight crenulations in the edge of the stumpy shapeless leg.

On the right hind foot are three much reduced and poorly differentiated digits. There is also an irregular scabbed lesion. The digits are bent so as to be pointed in the direction of the body, the direct opposite of their normal position. On the left front foot there is a large discolored and hemorrhagic lesion and two small papilla-like nodules in place of digits. It is not clear whether they represent structures that would have developed into claws on

normal digits, or whether they are the digits themselves.

Mouse 8869 is shown in Figure 18. In this case three digits are moderately well formed but are oriented peculiarly, some actual deformation of the bones themselves.

Figure 20 shows a left lateral view of the posterior end of Mouse 8235. Here, although the digits are more or less clearly

FIG. 16.

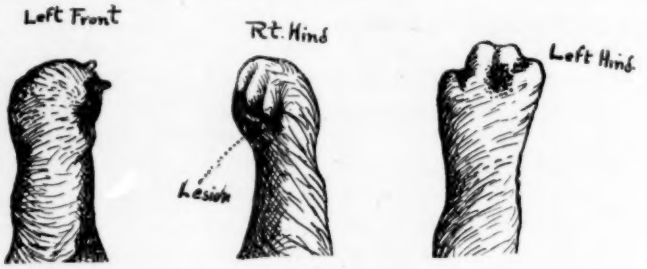

FIG. 17.

FIG. 16. Mouse 6107. A foot is shown with a slight abnormality associated with a hemorrhagic lesion.
FIG. 17. Mouse 6047. Three legs are here represented with markedly deformed digits. The abnormalities are associated with hemorrhagic lesions.

being twisted somewhat in the manner of those shown in Figure 17.

Figure 19 shows a ventral view of the posterior end of Mouse 7412. The right hind foot is shown from the ventral side defined, the whole leg is badly distorted and twisted into the extraordinary position in which it is shown. Of course it is impossible to estimate on the basis of superficial appearance what the bone and joint con-

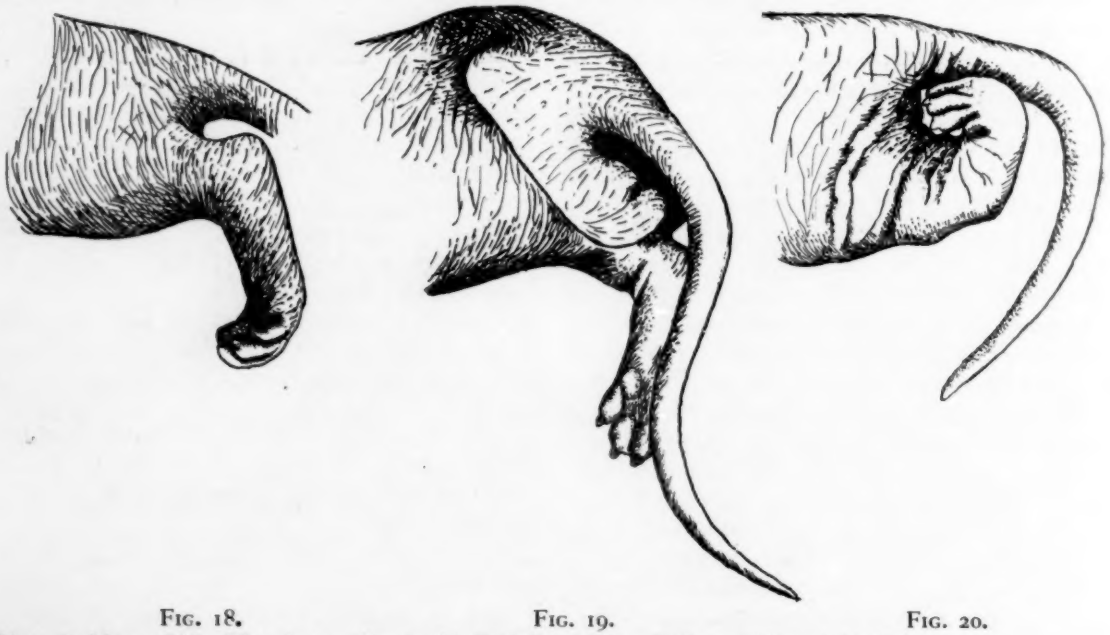

FIG. 18. FIG. 19. FIG. 20.

FIG. 18. Mouse 8869. The abnormality in this limb is mainly a faulty position of the digits.
FIG. 19. Mouse 7412. A ventral view of the posterior portion of the body showing an abnormally retracted and deformed left limb.
FIG. 20. Mouse 8235. Posterior portion of body showing a marked twisting and deformity of a hind limb.

and is normal. The left hind foot, however, is curled over toward the body and has no visible trace of digits. It is also almost certain that there is ankylosis, and possibly ditions actually are in this case, but it seems certain that they are markedly abnormal.

The above descriptions, although imperfect, will serve to show that the abnormal

leg condition is subject to wide variation. The breeding records shown in the various pedigrees mentioned later will further show that there are undoubtedly animals which are genetically abnormal-footed, but which somatically appear normal under a gross examination. We may now briefly consider

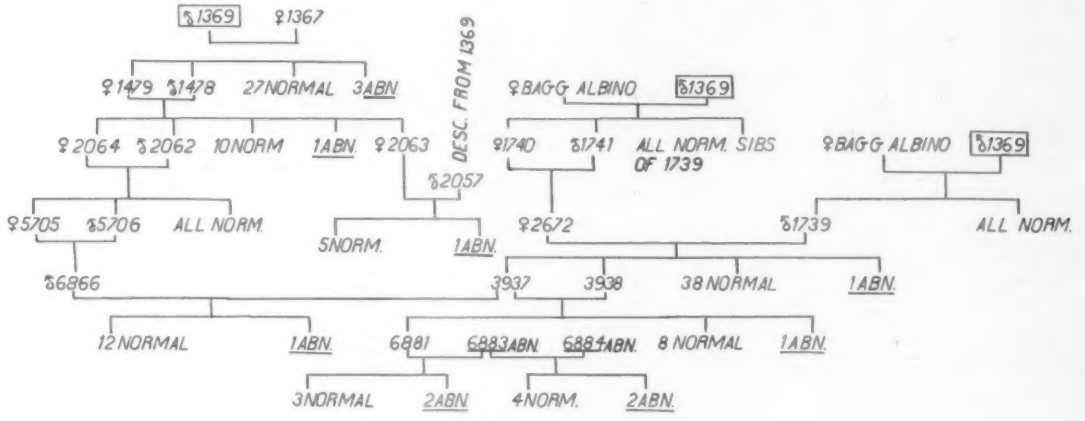
♂1369 ♀1367
♀1479 ♂1478 27 NORMAL 3 ABN.
DESC. FROM 1369
♀BAGG ALBINO ♂1369
♀2064 ♂2062 10 NORM 1 ABN. ♀2063
♀1740 ♂1741 ALL NORM. SIBS OF 1739
♀BAGG ALBINO ♂1369
♂2057
♀5705 ♂5706 ALL NORM.
5 NORM. 1 ABN.
♀2672
♂1739
ALL NORM.
♂6866
3937 3938 38 NORMAL 1 ABN.
12 NORMAL 1 ABN. 6881 6883 ABN. 6884 ABN. 8 NORMAL 1 ABN.
3 NORMAL 2 ABN 4 NORM. 2 ABN.

CHART I.

these pedigrees, which will be found in charts I to XI inclusive.

Chart I refers in four places to Mouse 1369. This mouse has been considered several times in the section on abnormal eyes. He was the male individual outcrossed with unrelated females to provide, for that character, the test of true inheri-

stock which was the parent stock for the outcross, it seems clear that Male 1369 introduced the abnormality in the outcross.

Chart II contains only animals that are descended from the outcross referred to. It will be seen that there are several abnormal-footed mice (15, to be exact) among them. Male 3492 is of interest, for by

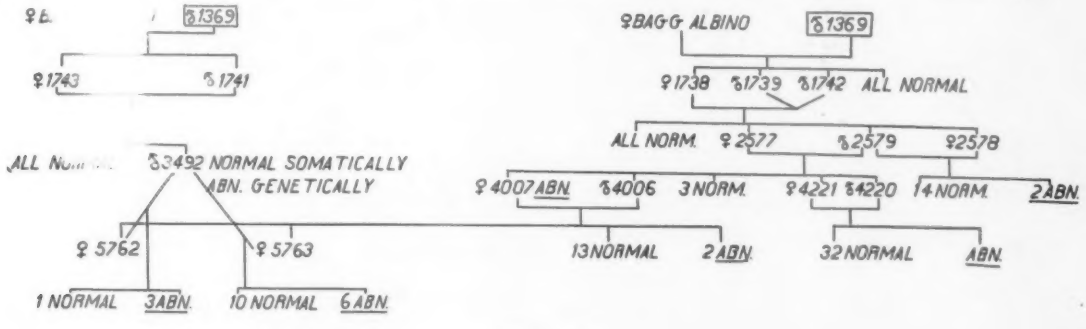
♀E. ♂1369
♀1743 ♂1741
♀BAGG ALBINO ♂1369
♀1738 ♂1739 ♂1742 ALL NORMAL
ALL NORM. ♀2577 ♂2579 ♀2578
♂3492 NORMAL SOMATICALLY ABN. GENETICALLY
♀4007 ABN. ♂4006 3 NORM. ♀4221 ♂4220 14 NORM. 2 ABN.
♀5762 ♀5763 13 NORMAL 2 ABN. 32 NORMAL ABN.
1 NORMAL 3 ABN. 10 NORMAL 6 ABN.

CHART II.

tance. The same crosses which were made in that case serve as well to provide the test of true inheritance for abnormal feet. Those in Chart I are the progeny of Female 2672 and Male 1739, and have among them 1 abnormal-footed animal. The further generations from that cross have actually 7 abnormal-footed individ-

Females 5762 and 5763 he gave a total of 11 normal and 9 abnormal young. Both these females and Male 3492 himself were normal in appearance. The proportion of abnormal-footed young suggests however, that either he was genetically abnormal while the females were normals carrying abnormal foot as a recessive, or

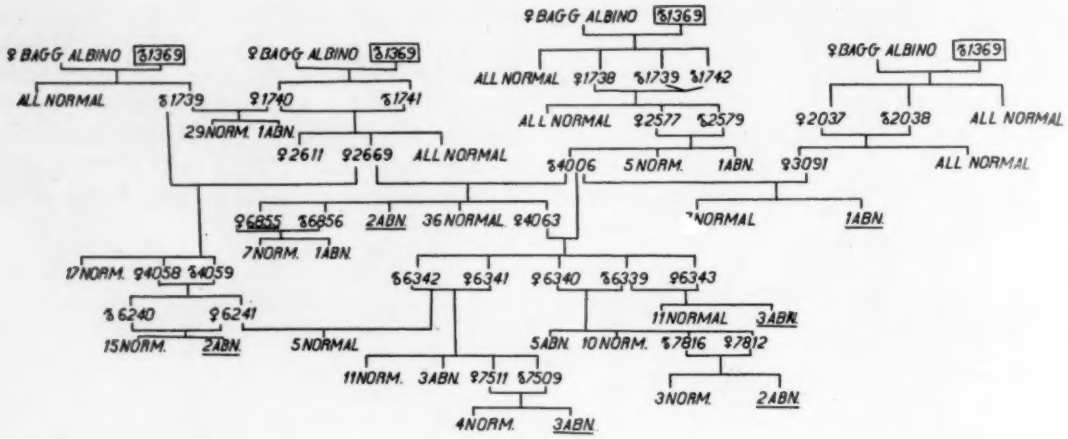

Chart III.

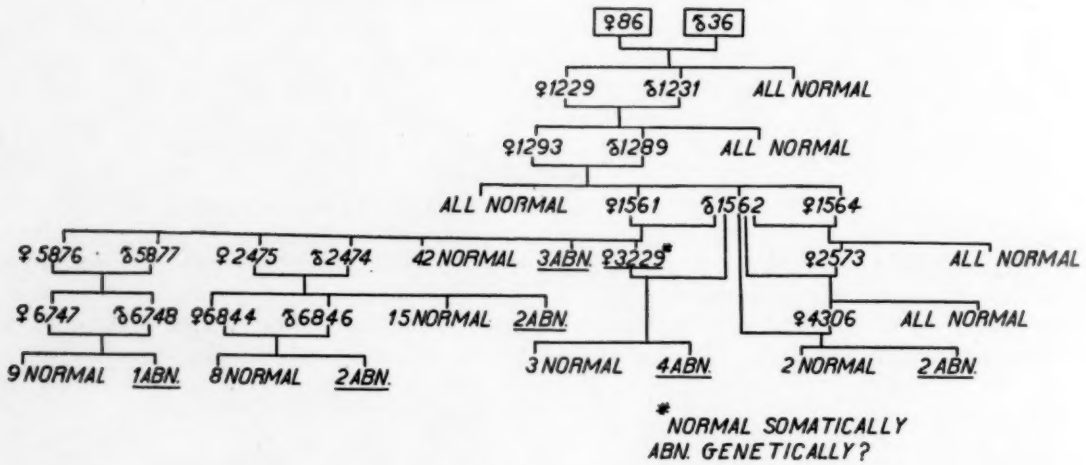
♀86 ♂36
♀1229 ♂1231 ALL NORMAL
♀1293 ♂1289 ALL NORMAL
ALL NORMAL ♀1561 ♂1562 ♀1564
♀5876 ♂5877 ♀2475 ♂2474 42 NORMAL 3 ABN. ♀3229*
♀2573 ALL NORMAL
♀6747 ♂6748 ♀6844 ♂6846 15 NORMAL 2 ABN.
♀4306 ALL NORMAL
9 NORMAL 1 ABN.
8 NORMAL 2 ABN.
3 NORMAL 4 ABN.
2 NORMAL 2 ABN.
* NORMAL SOMATICALLY
ABN. GENETICALLY?

Chart IV.

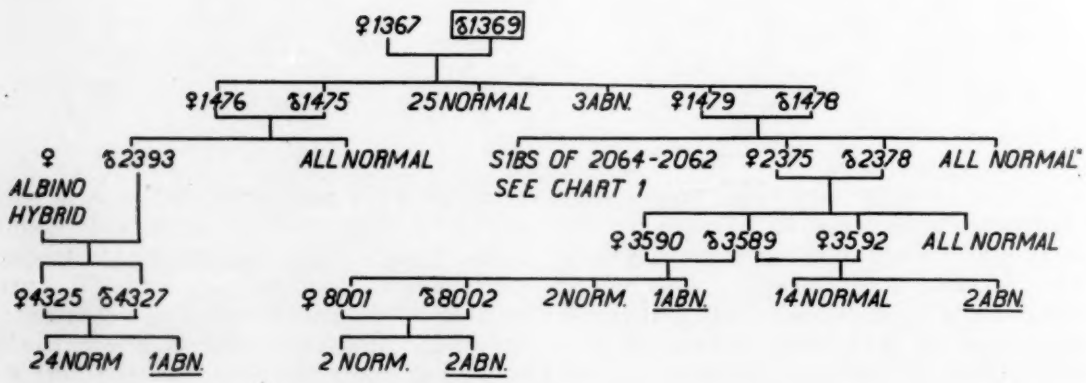

Chart V.

that both of the females were genetically abnormal although somatically normal and that he was a normal, carrying recessive abnormal foot. Of the two possibilities the former seems the more likely, for it requires that in one individual only, instead of two, would have to be present the usual condition of a "normal overlap."

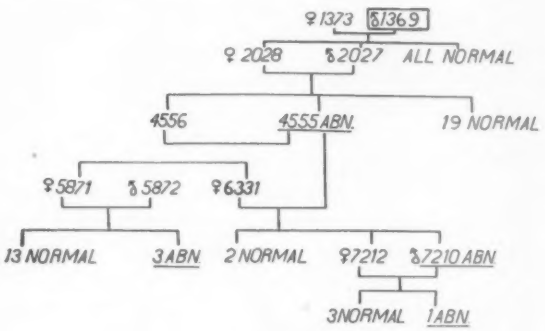

CHART VI.

These "overlaps" do not appear to be as frequent in the abnormal foot series as they are in the abnormal eye series.

Chart III shows extensively family descendants that are also from the original outcross. Although the numbers obtained from the cross of Female 7511 by Male 7509 are small, they suggest the possibility that one of these animals may have been a normal overlap and therefore genetically an abnormal.

On Chart IV is shown another entirely distinct family descended from a second pair of *x*-rayed mice, Female 86 and Male 36. The first abnormal-footed animals to appear were in the fourth generation. One of them, Female 3229, may possibly have been genetically abnormal although somatically normal, as her progeny consists of 3 normal and 4 abnormal young individuals, a close approximation to a 1:1 ratio.

Charts V and VI show two lines of matings giving abnormals, but confined to the original family in which No. 1369 himself appeared.

Female 1367 in Chart V was his sister and Female 1373 was his half-sister. Taken alone these two charts could not be used as proving inheritance, but in conjunction with the charts showing the outcross they indicate clearly that the abnormal-foot character was being inherited in this inbred stock and that Female 1367 carried the foot abnormality, while Female 1373 did not.

Chart VII shows what in some ways is a complicated line of descent from the outcross series: Female 6269 is one of the most likely cases on record of an animal somatically normal but genetically an abnormal. By two males, No. 6136 and No. 6237, she has given approximately equal numbers of normal and abnormal young. Although the numbers are small, the case seems to be fairly clear.

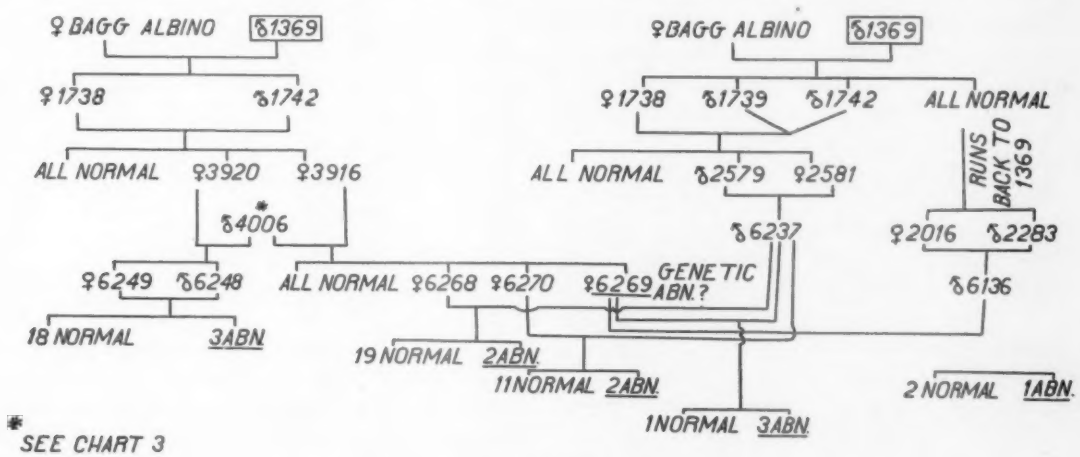

CHART VII.

Chart VIII brings us again to a series of matings all within the inbred line in which Nos. 1367, 1369 and 1373 originated. As proofs of the fact of inheritance, these

pedigrees are inadequate and must be supplemented by as careful and extensive experimental work along the line of an outcross as it is possible to carry out with the material available.

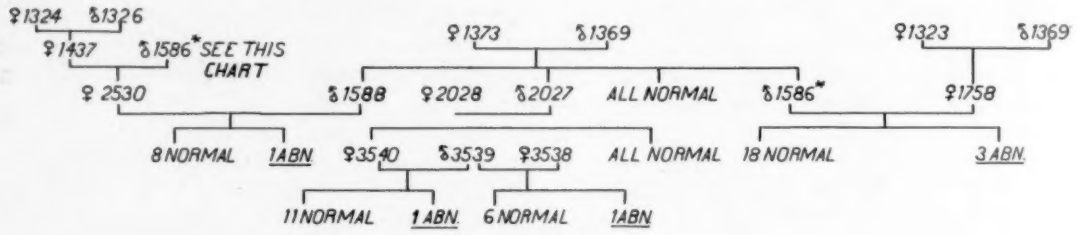

CHART VIII.

In one way, Chart IX presents evidence along the line of an outcross. The line

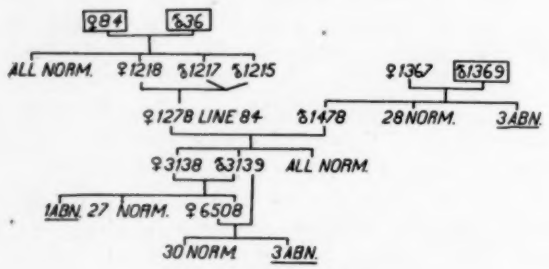

CHART IX.

used was one in which the ancestors had been *x*-rayed. The fact, however, that no young with abnormal feet have been born among the *inbred* descendants

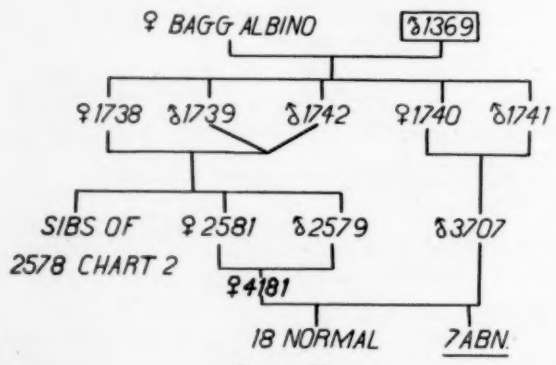

CHART X.

of Female 84 and Male 36 serves as evidence that the foot abnormalities have again been introduced by Male 1369, although it is not certain from which of his parents he and his sister Female 1367 derived them.

The reappearance in Chart IX of abnormals among the inbred descendants of Female 1278 and Male 1478 is an excellent supporting test of inheritance of the abnormal-foot condition.

Chart X is a small supplementary chart which might have been added to Chart II,

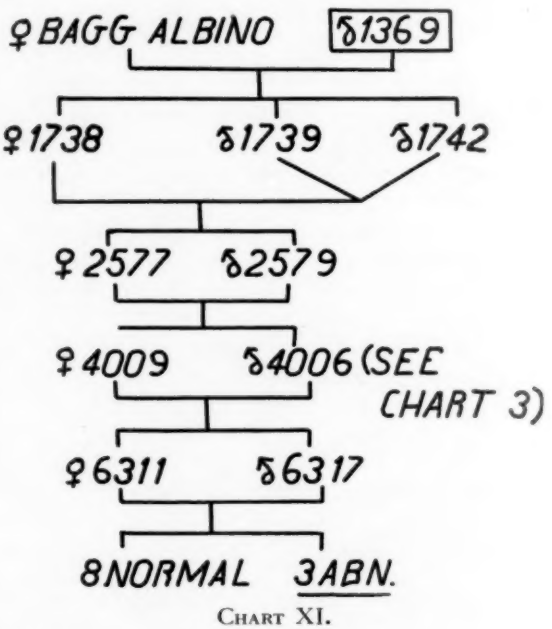

CHART XI.

but for the resulting confusion due to too many lines of descent. It presents no new features, being merely an excellent example of the action of the abnormality, which, after remaining unexpressed for four generations, suddenly appeared in the progeny of Female 4181 × Male 3707 in 7 animals.

Chart XI is another side line of the same general family. The pedigree in this case has been abbreviated and made diagrammatic in order to bring out the main point, namely, the appearance of the abnormality in the fifth generation, shown

in the *seventh* after the *x*-ray treatment was actually given.

To sum up these charts, we may say that there are four main points brought out by them:

1. A true test of inheritance of the foot abnormality is repeatedly shown by the outcrosses between females of the Bagg albino race with Male 1369.

2. A secondary test of inheritance is shown in Chart IX where an outcross with animals of *x*-ray (line 84) is shown.

3. The occurrence of the potentiality for giving abnormal feet is shown by Chart V to be present as far back as the F_1 (first) generation *after* the *x*-ray treatment was given.

4. Certain animals by their breeding behavior (Male 3492, Chart II, Female 3229, Chart IV, Female 6269, Chart VII) indicate the fact that they are somatically normal but genetically similar to a mouse with abnormal feet. This occurrence of "normal over-laps" is the common experience of those who investigate the inheritance of structural characters in birds and mammals.

DISCUSSION

There are certain aspects of the experiment herein described which are worthy of careful consideration from a general medical and therapeutic viewpoint. Thus, if we are right in assuming that the eye abnormalities which we have been considering are the result of a change in the germ plasm induced by treatment of adult mice with *x*-rays, several conclusions follow.

The first of these is that although the somatic tissues of the treated mice themselves show no gross histological changes, there has been an effect on the germ plasm. This effect has resulted in a genetic change which is inherited. Its inheritance is orderly and mendelian. Its somatic manifestation is an abnormality of the optic nerves and eyes. This all suggests, of course, the need of extreme caution in the use of *x*-rays for medical purposes when the individual treated is of reproductive age or younger.

In the case of neoplasms, where the situation is serious, there seems naturally little reason why *x*-ray treatment should be curtailed. For purposes of temporary sterilization, the use of the *x*-ray appears to the writers to be a tremendous risk. While the treatment of the individual case might result most satisfactorily, the desired results being promptly and successfully obtained, the possibility of influencing the progeny by producing hereditary changes in the germ plasm cannot be ignored. Because of the long time interval between human generations, the immediate result, rather than the influencing of the germ plasm, has come to be our natural viewpoint. This viewpoint will, either directly or indirectly, be the worst enemy of an experimental test like the one here described. For this reason, if for no other, it is unfortunate that the medical men interested in the application of *x*-ray treatment to other than cancer cases, cannot see the experimental results themselves. The clear and striking abnormality must lose force in description.

It should be noted in passing that none of the work here reported indicates that *x*-ray photography as at present practiced in the medical and dental professions is harmful. Of course, the region photographed and the intensity and duration of the exposure will determine this factor to a large degree.

It would be highly desirable to conduct a series of experiments on the radiation of various portions of the body, and to study what genetic effects, if any, are produced. Since in our work the exposure was over the whole dorsal surface, there are no data that bear on this matter of localization. Fraenkel describes the treatment of the heads of guinea-pigs with *x*-rays, and the subsequent appearance of hairless areas on the head, not only in the treated animals, but in their progeny.

If confirmed with larger numbers and carefully controlled genetic stock, this finding is of prime importance, for here the effect on the germ plasm would necessarily have been secondary to the direct effect on the soma (head). This looks far more like inheritance of an acquired character, while our results appear to be in the nature of a *direct* effect.

The work of Mavor on Drosophila has also shown that the distribution of the chromosomes at maturation may be influenced by *x*-rays. The result of this is the production of non-disjunction of the sex chromosome. This condition appears to be inherited. The effect, however, may be primarily on the cytoplasm, and the result of a change occurring there may well be imagined to show itself in the distribution of whole chromosomes or other abnormalities of the mitotic process.

As before mentioned, the experiments of Blakeslee and Gager are also probably explicable along this same general line of reasoning.

The orderly behavior of the eye abnormality here recorded suggests, however, that in this case a single gene, or a small area of the chromosome, has been affected. There is, as we have stated, no evidence of the inheritance of an "acquired" character to be derived from this experiment with mice. It appears to be a direct effect on the germ plasm itself.

It is interesting to note in passing that Guyer and Smith, in their experiments on the production of lens antibodies in rabbits, are inclined at least to consider that the inheritance of an acquired character is involved. Without wishing to detract from the great merit of their work, it should, it seems, be pointed out that the pedigrees which they have published in their papers in the *Journal of Experimental Zoölogy* show undoubted *transmission* of some sort of tendency to defect, but so far as we can see, they contain no actual test of true inheritance of the type referred to above under the headings of both eye and foot abnormalities. In every case that we have noticed, Guyer's pedigrees show either a chance for transmission by the female, or else a cross with an actually abnormal male individual. Here, of course, a great amount of actual material besides the sperm itself is introduced from the abnormal male into the body of the female and affords at least a possibility of direct transmission of some agent causing the abnormality.

In closing, therefore, we should like to review briefly what we believe to be the important points in the results here reported:

1. Abnormalities of the eyes and feet have first appeared among the second and third generation descendants of mice which as adults had been given one-fifth of a human erythemal dose of *x*-rays on each of five successive days.

2. The first young were obtained from treated animals as late as ten weeks after their treatment, thus insuring no in utero effects.

3. The eye abnormality is inherited as a mendelian recessive character.

4. The foot abnormality is also inherited, but as yet the exact nature of its inheritance has not been worked out.

5. The fact of the appearance of these abnormalities, the clear lesions involved in their somatic expression, their absence from the control animals, and the work of others who have used the physical agents lead us to believe that the *x*-ray treatment has had a causative effect upon their production.

6. This effect appears to be of the nature of a direct effect on the germ cells themselves, not *through* the soma as an acquired character.

7. The experiments here recorded justify, we believe, the recommendation of extreme caution in the use of radium or *x*-ray therapy on human individuals who are likely ever to serve as parents after they have been treated.

8. This caution should be practiced until the whole matter of the effect of *x*-rays and radium on the germ plasm has been much further investigated than at present.

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FORCEPS FOR CLEANING RADIUM NEEDLES AND TUBES

BY J. S. ULLMAN, M.D.

NATCHEZ, MISSISSIPPI

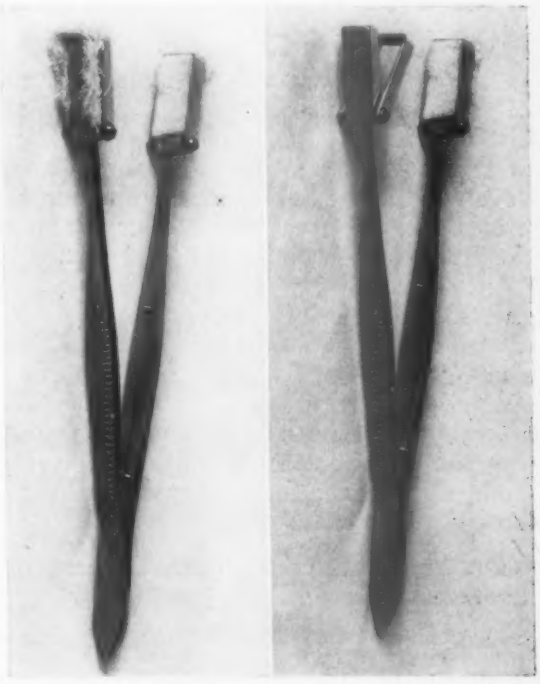
THIS instrument was devised as an additional means of protection for the therapist and technician. It has always been apparent to workers with radium that a very appreciable danger lies in drawing the container between the fingers when they are covered with nothing but a few layers of cloth.

It will be seen that this apparatus will add considerably to the convenience and efficiency of the technician, for to try to hold a needle on the table with ordinary forceps while mopping with another pair of forceps is a most cumbersome procedure at best.

It will be seen that the instrument is an adaptation of the embroidery hoop and consists of a pair of ordinary anatomical forceps on the ends of which have been fixed rectangular plates, the edges of these plates being turned back to give rigidity. Bands of very light spring metal are fitted around the turned-back edges and fastened by through and through pins to the proximal ends of the plates in such fashion that the pins may be lifted up for the insertion of gauze or other cleansing fabric. Obviously the bands are returned to the proper position along the edges of the plates and finally hold the material to be used for wiping or polishing a tube or needle.

Ordinary surgical gauze may be used for drying the radium containers. By adding oil and emery flour to the surface of the gauze, or by using some abrasive cloth, the instrument becomes a most efficient means for polishing the container.

Anyone who has tried to clean dental compound from containers knows that considerable effort is required to remove this material. A fine abrasive applied in this manner, however, does this work better than anything else known to the writer.



It will be seen from the illustration that this instrument is simple in its construction and use. So far as is known to the writer it is the only thing of the kind to protect the therapist and technician.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Information of interest to all readers and lists of officers of The American Roentgen Ray Society and The American Radium Society will be found on the two pages preceding Table of Contents.

FIFTH ANNUAL MEETING EASTERN SECTION AMERICAN ROENTGEN RAY SOCIETY

CHALFONTE-HADDON HALL, ATLANTIC CITY, N. J., JANUARY 24–26, 1924

THE CHICAGO MEETING

Among the twenty-four annual meetings of the American Roentgen Ray Society the last meeting at Chicago stands out as one of the most interesting. This interest was developed along several lines, but perhaps was most apparent in connection with the papers pertaining to therapy. This was indicated by the large number of guests and members taking part in the discussions. The address by Dr. Robert Knox of London, England, was one of the outstanding features of the meeting. The attendance of both members and guests was the largest recorded in recent years. Besides Dr. Knox there were several other foreign guests, among whom were:

Dr. Arthur Burrows, Manchester, England.

Dr. Alfred G. Dominguez, Havana, Cuba.

Dr. J. Stanley Ellis, Shantung, China.

Dr. Carlos Johnson, Havana, Cuba.

Dr. Jose Ochotorena, Havana, Cuba.

Dr. Filiberto Rivero, Havana, Cuba.

Dr. Carlos Heuser, Buenos Aires, S. A.

Dr. Paul Hodges, Peking, China.

The scientific and commercial exhibits were large, and much that was new and interesting was shown.

The officers elected for the ensuing year were:

President-Elect: Dr. George W. Holmes, Boston, Mass.

First Vice-President: Dr. Frederick M. Law, New York, N. Y.

Second Vice-President: Dr. Ernest C. Samuel, New Orleans, La.

Secretary: Dr. W. Warner Watkins, Phoenix, Ariz.

Treasurer: Dr. William A. Evans, Detroit, Mich.

Librarian: H. W. Dachtler, Toledo, O.

Member of Executive Council: Dr. Harry M. Imboden, New York, N. Y.

With this number of the Journal the present editor terminates his official relations with it. While the various tasks of the office have at times seemed exceedingly difficult, even unsurmountable, they have not been without proper and due compensation in the form of unusually close relationships which were developed not only with the various members of the Society but with foreign correspondents

and other editors. The emotions which one experiences upon such an occasion are of mingled regret and relief; regret in laying down work which has become part of one's routine, and in the severing of some of the choicest relationships; relief that the time which was devoted to the Journal may now be devoted to other fields, and also in the thought that the Society has entrusted the future of the Journal to hands which have been tried in various fields and never found wanting. It is to be hoped that the members will accord to the new editor even a greater degree of cooperation and support than was given the present one. If this is done, his lot, indeed, will be cast in pleasant places and the future of the Journal will be assured. Gratitude for invaluable assistance is extended to the associate editors, Dr. William Duane, Dr. Henry K. Pancoast and Dr. James T. Case.

CORRESPONDENCE

To the Editor:

I have completed my work in connection with the raising of the memorial fund for Dr. Van Zwaluwenburg. The total subscriptions received amount to $2972.50. The money was invested from time to time, and the total earnings amount to $153.46. I am turning over today to the treasurer of the University of Michigan for permanent investment this total, $3125.96.

Very sincerely yours,
WM. A. EVANS.

Subscribers to THE AMERICAN JOURNAL OF ROENTGENOLOGY *visiting New York City, are invited to make the office of* THE JOURNAL (69 *East 59th Street, New York*) *their headquarters. Mail, packages or baggage may be addressed in our care. Hotel reservations will gladly be made for those advising us in advance; in this case, kindly notify us in detail as to requirements and prices. List of operations in New York hospitals on file in our office daily.*

BOOK REVIEWS

PRINCIPLES OF *X*-RAY AND RADIUM DOSAGE. By Albert Bachem, Ph.D. Cloth, Price, $8. Pp. 274, with 67 figures. Chicago: Albert Bachem, 1923.

X-ray and radium therapy have had careers of ups and downs similar in many respects to other therapeutic measures, but it seems at the present time that they are both in the process of settling. This is due to the fact that the biological factors of radiation have been extensively studied and are fairly well known while the limitations of the applications of deep *x*-ray therapy and radium may be considered as not yet conclusive. This book, therefore, comes at a very fortunate time, as it contains the underlying principles of radiation, discussing such important problems as the determination and measurement of quantity by radiation, the definition and measurement of quality, the distribution of various kinds of rays in different media and a very important chapter on practical dosage. The author draws largely on literature which has been very voluminous in the past five years and tempers his conclusion with his own experiences. This book merits the serious consideration of all interested in deep roentgen and radium therapy.

FIRST AID *X*-RAY ATLAS OF THE ARTERIES. By H. C. Orrin. Cloth, Price, $1.00. Pp. 46, with 9 illustrations. New York: Paul B. Hoeber, Inc., 1923.

This small atlas is intended to give a conception of the arteries of the body, especially in their relationship to the bones. The plates, while small, are very satisfactory and should be of service to first-aid students as well as to nurses.

PHYSIOTHERAPY TECHNIC. A MANUAL OF APPLIED PHYSICS. By C. M. Sampson, M.D. Cloth. Price, $6.50. Pp. 443, with 85 illustrations. St. Louis: C. V. Mosby Co., 1923.

Of all opportunities given to men to investigate somewhat unknown fields, those taken advantage of by Dr. Sampson have amounted to such a volume that his observations of the necessities of technique are really most important. This book gives particularly good descriptions of the real technique in physiotherapy. This first edition, however, is really "padded" with unnecessary parts, for doctors do not need to be told how to examine patients. The many anecdotes and personal examples in the book are interesting but unnecessary; also his various disagreements with other Army doctors. Aside from these extraneous thoughts, the real "meat" of his book is good. This applies especially to his explanation of high-frequency electricity and the technique and applications used in diathermy.

The chapter on Indirect Diathermia or the Use of the Non-vacuum Electrode is to be commended because it omits any consideration of the vacuum electrode now popularized as the "violet ray." This "violet ray" is one of the greatest detriments to electrotherapy that has ever been foisted on the public.

The chapter on Static Modalities brings forth many truths of static electricity which have never been sufficiently emphasized.

Actinotherapy and phototherapy are both very well presented, and though it is evident that Dr. Sampson was quite successful in the treatment of *x*-ray burns, he lays almost too much stress on this work.

The use of galvanic, faradic and sinusoidal currents is well explained and brought forth.

Massage and hydrotherapy are given a good modern exposition and the new form of hydrotherapy, namely the whirlpool baths, is explained.

The most necessary chapter is called Trouble Shooting and should certainly be included in any book on technique, though Dr. Sampson is the first to think of such a separate chapter.

On the whole, this book is worth while in the strictly scientific and technical parts, and it is a step in the right direction to show that scientific application of physiotherapy is an aid to established medical and surgical treatment of disease.

N. E. T.

TRANSLATIONS & ABSTRACTS

Conclusion of Abstract of Proceedings of Meeting held at Heidelberg, May 26–27, 1923.

Döderlein (Munich). The therapy of gynecological cancer with radioactive substances. Whether the radioactive substances radium and mesothorium are in their effect identical with each other and with the roentgen rays, has not been definitely established. They have the advantage over roentgen rays of emitting rays harder than can be produced by any roentgen apparatus so far designed. Their disadvantage is that their application is quite limited locally. On the other hand, their application requires less of the operator's time, and aside from their great initial expense, they are cheaper to use. Since the life of radium is reckoned as eighteen hundred years, while that of mesothorium is only twenty years, it is not established that mesothorium does not, on account of its more rapid decomposition, have an effect different from that of radium.

With these substances there have been treated in the Munich University Frauenklinik in the years 1912–1918, 1016 cancerous women. These cases included 962 carcinomata of the female genitals.

Predominant among these was cervical carcinoma, with 755 cases. It is now more than five years since the treatment of these patients was finished, so that Winter's statistical requirement has been satisfied. Of these 755 patients, 103, or 13.2 per cent, are living and apparently cured.

When one considers that the results of the radical abdominal or vaginal extirpation of the carcinomatous uterus show, for all operations, an absolute percentage of cures of 20 to 25, one might estimate the curative power of radiation treatment as only about half that of surgical. This, however, would be a fallacy, and would hinder scientific progress; for it is to be considered that radiation treatment is used upon much more unfavorable material than is surgical, which naturally holds down the percentage of cures. This is confirmed by a comparison of the percentage of operability in the material in question with that previously seen. While the author used to operate on from 60 to 70 per cent of the carcinomata of the uterus which came to him, this material, 755 patients, included only 110 operable cases, at operability percentage of 14.58.

Of these 110 cases, designated as Group I, 48 have been cured by treatment with radioactive substances, that is, on recent follow-up more than five years after the end of treatment, there were found alive and well 43.6 per cent.

In Group II, comprising the so-called "borderline cases," in which the possibility of surgical extirpation could be entertained, there were 136 patients, of whom 31, or 22 per cent, have been cured.

In Group III were 340 patients too far gone for any possibility of radical extirpation. Of these, 23, or 6.7 per cent, have been cured; and of the 169 patients in Group IV, hopeless cases, one has been cured.

The author believes that in estimating the value of cancer treatment in the future, the quality as well as the quantity of the material will have to be considered.

These figures represent the minimum value of radiant therapy, for in the first years of the method to which they correspond, the technique was being developed and the correct dosage had to be learned. A lamentable feature of radiation treatment is that the patients have to be seen a number of times, and not seldom the improvement is so prompt that they do not return for the full course. Such insufficient treatment naturally depresses the showing for the method, without constituting any evidence as to its lack of value, just as in syphilis one can designate salvarsan as a useless drug because there are cases in which its incorrect use has led to no result. If one excludes from the foregoing statistics those cases in which the treatment was incomplete, in which there were not at least three sittings, we have the following showing:

Group I 62 cases, 46 cured, or 73.6 per cent; Group II 75 cases, 31 cured, or 41.2 per cent; Group III 176 cases, 23 cured, or 13.1 per cent.

These figures may be regarded as showing the maximum result for the present-day treatment of carcinoma of the cervix with radioactive substances.

In the same period the author has treated 47 cases of carcinoma of the body of the uterus, with 11 cures. Of these 47 cases, 24 were operable, and only in these was a cure obtained; the 23 inoperable cases were all lost. In connection with the discovery, made in collaboration with the pathologic department, that the adenocarcinoma is resistant to radiation, the unfavorable results with the carcinoma of the body of the uterus appear to be explained by the lack of sensitivity of the gland-carcinoma. It is likely that this will alter our attitude in the treatment of carcinoma of the body.

Of recidiv following operation elsewhere, the author saw in the period in question 57 cases. Not one of these patients was living after five years. According to the joint experience of the surgical, dermatologic and pathologic

departments, which have observed rapid extension of the carcinoma after diagnostic excision, this lamentable characteristic of recidiv appears in a new light: in all local recidiv cases, the operation is only a great diagnostic excision, and if even a small incision into the carcinoma will make the cells run wild, it is plain that biologic alteration of the carcinoma cells in consequence of operative interference will render these cells resistant to radiation. The author warned against this years ago, and believes that in view of the results of radiation alone, we should in the future withhold surgery where the carcinoma is accessible to radiation.

The remaining results with the author's material are as follows:

Of 65 cases of vaginal carcinoma, none has been cured by radiation. It appears, that in these cases the growth extends so rapidly into the surrounding tissues that the radiation therapy, like the operative, has as yet been unable to produce any result.

Likewise, poor results were obtained in 14 cases of carcinoma of the ovary. They were all operated upon, since it is naturally out of the question to handle such large tumors by radiation alone. Only one case has been cured.

Of 17 cases of carcinoma of the vulva, only one case has been cured, of 7 carcinomata of the urethra, none. Here the radiation treatment fails as well as the operative.

These results make it all the more worth while to try to sensitize the carcinoma in various ways, perhaps even through radiation of the hypophysis.

In confirmation of the conception that radiation has a selective effect, the author points not only to the anatomical investigations upon the alterations in the carcinoma cells following radiation, but especially to a case which he has already described (*Münchcn. med. Wchnschr.*, 1922, No. 7). This deals with a woman thirty-one years old who in 1913 developed a rapidly growing carcinoma of the portio, which was so favorably influenced by radiation that on April 12, 1919, she gave birth to a fully developed living child. In this case the diseased organ was so completely restored to normal that not only its anatomic structure but its biologic function was not entirely free from damage.

Wintz (Erlangen). Experience with roentgen therapy of cancer in the erlanger frauenklinik. The action of radium is limited to a depth of 3 to 4 cm. Radium is indeed biologically potent, but amounts sufficient to compare in effect with *x*-rays are not to be had. Seitz and Wintz formerly combined radium and roentgen rays, but in the last three years Wintz has treated portio-carcinoma with roentgen rays alone, and recently has used (ionic) copper as an adjuvant. Only in cases in which an adequate dose was given was there regression; at least 90, often 110 per cent of the single skin dose has been necessary. But while we here have a fundamental principle for the destruction of the carcinoma, we still have not the key to the healing process; this is a biologic moment which we have not yet mastered, though we have extensive destruction-methods at our command. Destruction and restitutio ad integrum, however, are not one and the same thing.

As for technique, Wintz uses one vulva field, two abdominal fields, one anal field, and two dorsal fields. Then the parametrium is radiated. In twelve weeks if the tumor has not vanished, there has been a fault in the technique. But the disappearance of the tumor does not mean a cure. The dosage remains the deciding factor.

With the aid of ionic copper, results are attained which surpass those of roentgen rays alone. The copper salts are driven into the tumor mass by cataphoresis, as well in the parametrium as in the portio. Appropriate disposition of the cathode and anode deposits much copper in the tumor, little in the skin. Among the unfavorable effects, vascular injuries are frequent. Double the erythema dose leads to induration of the skin, which resolves in from one to two years and which must not be interfered with, except perhaps for the application of heat. Furthermore, a damage of the vault of the bladder is often observed, and the bladder must therefore be empty at the time of treatment. Also, a tendency to calculus formation in the bladder is seen.

Every place that has had half a roentgen dose (skin, intestine, etc.) is to be regarded as a locus minoris; here a slight trauma suffices to cause damage, e.g., the pressure of a corset, etc. Diagnostic excision is the worst of all, and the author warns against it.

In carcinoma of the breast he uses large fields at a distance, 120 to 150 cm. skin-focus distance, through 3 mm. of aluminum. Deep radiation damages the lungs and causes induration of the pleura.

Statistics. Carcinoma of the portio: 15 per cent free after four years. Carcinoma of the breast: 4 out of 17 cases free five years; 7 out of 12 free four years; 19 out of 47 cases free three years.

Sachs (Heidelberg). The New Methods of Serodiagnosis of Cancer. The experimental attempts of the last ten years to immunize animals against cancer material by the use of cancer serum have failed. This has limited the hope of a serodiagnosis of cancer. Abder-

halden's theory of the excavation of organs by cancer by means of ferments has not been confirmed by Sachs and Oettlingen. Kottmann (Bern) has a method different from Abderhalden's, but he, too, has failed to obtain clear, practical and useful results. The fixation of complement in tumor diagnosis deserves looking into. The serum of patients who have tumors frequently gives a falsely positive reaction for lues. Lability of the blood proteins in pregnancy, infectious diseases and tumors gives rise to chemical methods of investigation. The determination of the antitrypsin content gives unreliable results.

Alterations in the serum of tumor patients can nevertheless be found in the overwhelming majority of cases. The similarity of the sera of pregnant women, patients with infectious disease, and with tumors, is significant: the cause is excessive tissue growth and tissue destruction. More to our purpose would be a reaction which would occur in only 30 per cent of cases, if it would occur only in the presence of a tumor.

There is thus no characteristic serodiagnosis for tumors; there are symptomatic reactions, which serve as aids. The question whether it is possible ever to discover a serodiagnosis of cancer is still an open one.

Kahn (Altona): A simple flocculation reaction associated with malignant tumors. During investigations upon the applicability of the varying inhibiting power of various sera toward hemolysis with sodium oleate for the differential diagnosis of malignant tumors, it was found that especially in tumor patients the decrease of the power to inhibit sodium oleate hemolysis parallels a degree of cloudiness which appears some time after the serum and oleate are brought together. Technique: Six test tubes, in each of which are 0.2 c.c. of serum, then 0.2 c.c. of glycerin, and in increments of 0.05 c.c., 0.2 to 0.4 c.c. of sodium oleate solution. Cloudiness or flocculation is then read off. The reaction was positive in all cases examined of carcinoma of the gastrointestinal tract, the liver and the pancreas; with the exception of a case of carcinoma of the pancreas with severe cholemia. It was otherwise positive only in cases of highly febrile tuberculosis, in several cases of highly febrile acute infections, and in extensive cirrhosis of the liver. These do not influence the practical application of the reaction, for these conditions may be distinguished clinically. It cannot be theoretically regarded that this has to do with specific immunity reaction.

The advantage of the reaction over the old hemolysis methods and the meiostagmin reaction is that while the exactness is about the same, the manipulation is considerably simpler.

A positive reaction consists in the appearance of flocculation after the addition of 0.25 c.c., of cloudiness after 0.3 c.c. of the neutralized 0.1 per cent oleic acid solution.

Caspary (Frankfurt-on-Main): Cancer and immunity.

The methods of producing unspecific immunity are manifold. It can be induced by parenteral injection of foreign proteins, tissue autolysates, blood transfusion, implantation of embryonal tissue, chemicals, protoplasmic poisons, and especially by complex metal salts. Coincident with cell destruction there appear effects from small doses of roentgen rays; likewise from fevers. Even dyspnea sets immunity processes in motion. The percentage of fatal cases in men who do bodily labor is smaller than in those who do not. The catabolism of cells increases the resistance. According to the necrohormone theory, the stimulation of the necrohormone causes growth of connective tissue: hence the defensive process of the body. First the lymphocytes appear at the disease-focus, and are there transformed into fibroblasts. The process is identical with scar-formation. The best effect for immunization is obtained by the introduction of any kind of tissue. The first degree of the effect is a lengthening of the latent period and better tolerance of the tumor. The second degree is marked by a definite hindering of the growth.

So far there is no prospect of these consequences of therapy being available in man. Diathermy produces a local increase in temperature and can thus be of use. The production of fever leads to weakness. Injection of metal salts has only an adjuvant effect. Roentgenotherapy. Little is to be expected from passive immunization. Experiments upon immunity processes can yield us practical means for therapy.

Werner (Heidelberg). The new biologic and chemotherapeutic methods of treating cancer.

Despite operation and radiation, more than 85 per cent of cancer patients die. The biologic and chemotherapeutic procedures are regarded as either strengthening of the radiation effect or delaying postoperative recidiv or else as independent measures. The object is always an influencing of the blood or lymphatic channels or the tumor cells themselves in the sense of a destruction or of a resistance of the region of the endocrine organs.

It is seldom that there is an attempt to utilize the chemical affinity of tumor cells for an injected substance. There is, however, often an indirect effect, by reducing the blood supply or by the stimulation of endocrine

organs. Chemical therapy in the strict sense comprises the use of clinically tested preparations of arsenic, iodine, silicon, silver, copper, iron, selenium,vanadium, and lead; and further, the use of vital stains.

For chronic use, arsenic is employed in small or medium-sized doses; upon the application of large doses, many lymphosarcomata heal, likewise myelogenous bone tumors, and skin cancers. Intravenous injection of large doses of atoxyl, salvarsan, or related preparations is followed by rapid melting away of even large sarcomata, but at the price of a stormy general reaction that is not free from danger.

Intratumoral injection of potassium iodide for the purpose of making more effective the radiation is disappointing.

Silicon occupies a place not only in folk medicine, but also in the form of various combinations for use by mouth or by injection as true or colloidal solutions. Isolated examples of its successful use in confirmed carcinoma have been described, but the single trial of the author was negative.

Silver and copper salts are given either intravenously or intratumorally, in the hope of destroying the tumor cells or of strengthening the effect of radiation, or for the indirect effect through the blood. The preparations most frequently used are collargol, argatoxyl, fulmargin and argoflavin; and of the silver salts, cuprase of the copper. Again, only isolated results are attained, at the price of severe constitutional reactions. Wintz has used copper intratumorally and believes that it increases the radiation effect.

Selenium operates, in the combinations so far tried, as does a rsenic, but the dosage is difficult, and large doses produce mild intoxications; moreover, the tolerance of difference individuals appears to be very different. The form best withstood the colloidal selenium-vanadium. Some carcinomata of the gastro-intestinal tract have shown apparently good results.

Iron is used principally for the betterment of the blood-picture. In secondary anemia and beginning cachexia an especially favorable effect is seen. It is particularly important to give this aid for the constitution before radiation.

The acetate of lead, which has been recently recommended on all sides was tried by the author fifteen years ago, and has not proved of value.

Vital stains, especially methylene blue and methyl violet, stain the tumor intensely, but have little application in combination with radiation. Roosen has devised an interesting method of giving subcutaneously methylene blue, which stains the tumor and the body tissues; the body tissues soon become decolorized, but the tumor does not; the administration of calomel is then expected to produce bichloride of mercury in the tumor. Or, isamin blue is injected until it stains the tumor deeply, and then neosalvarsan is injected to produce toxic oxidation products in the tumor. Unfortunately these two methods have not produced convincing results.

Injection of cholin compounds sensitizes the tumor to radiation, but it also sensitizes the skin, so that as yet no advantage has been derived from it.

The injection of protein bodies, e.g., casein compounds, has a definite effect for the better on the general state of the patient, but little effect on the tumor itself. The effect of bodies given to increase the lymphocytes, e.g., sodium nucleinate, is not much different.

On the other hand, one sees that, with the intravenous injection of foregoing or even any kind of sera, organ extracts, expressed tissue juices, and autolysites of tumors, either similar to or different from the tumor treated, have a good effect on the tumor, especially at the beginning of treatment, and sometimes there is a considerable diminution of the size of the tumor. As a rule the failure of the treatment is observed in four to five weeks. One can hope, however, for a new therapeutic weapon with the development of the method. How far one can hope for results by combinations of these procedures, and especially by increasing the doses, is still quite uncertain.

In the sense of protein-therapy, such remedies as the antimeristem of Schmidt, or cirrhosan, give some effect, but the experiences so far have yielded but little.

In some cases there have been seen apparent healing of hopelessly sick patients, giving the impression of a therapia sterilisans magna. As an example, a single intravenous injection of sterile filtered milk has been followed by the complete disappearance of an histologically demonstrated large carcinoma of the stomach.

We cannot count on these results unqualifiedly, because special circumstances of unknown kinds, beyond our control, e.g., the accidental admixture of bacterial products and the like, make it impossible to reproduce the conditions of a given case.

Erdmann (Berlin). Cultivation of tumor cells.

Epithelial cells can be cultivated in vitro without limit, if they are transplanted every second day. The medium must be semi-solid; if it becomes fluid it must be replaced at once. The cancer cells must be transplanted every twenty-four hours or oftener. This is

why the cultivation of cancer cells is difficult. Normal cells from birds and mammals which grow without limit in vitro, die promptly when transplanted to a new host, in contrast to the inoculated tumors. Experiments are under way to reduce the resistance of the prospective host. An inoculated tumor continues only when stroma is inoculated with it. This calls renewed attention to the study of the stroma. But if too much connective tissue is present, the epithelial cells do not grow. The growth of epithelium is thus something secondary; it is linked up with the connective tissue stroma in some way.

Ellinger, Gans and Rapp (Heidelberg). Thorium nitrate as a means of sensitizing.

Starting from the standpoint that only the absorbed portion of the rays is effective, it was sought to permeate the tumor tissue with a substance of high atomic weight in the finest possible state of division. The substance had to be non-toxic. Thorium nitrate in 10 per cent solution together with 12 per cent of cocaine was injected into the tumor or the lupus tissue, and radiation applied. The injection is very painful, the pain lasting from half an hour to twelve hours. Injection of large tumors requires narcosis. Contrary to the usual roentgen handling, one begins with smaller doses, and should not exceed a third of the single skin dose. The increase of the effects is to be explained by the effect of the secondary electrons in the tissue. The method is danger-free with small amounts of the ray; with larger amounts there is rapid destruction. No fatalities.

Gynecologic Congress in Heidelberg. Section of Radiation Therapeutics, May 25, 1923.

Risse (Freiburg). Blood changes after radiation.

The author found in cases of carcinoma an acceleration of the decrease of the blood cells, but after radiation, usually a slower decrease, which lasted for six to eight weeks. Similarly, an increase in the cholesterin and lecithin content of the blood. In the majority of cases, after an initial hyperglycemia, there was a decrease of blood sugar. The values sank to as low as one tenth. In radiated diabetics the sugar in the urine decreased, but the sugar content of the blood remained unchanged. This was true of radium radiation as well as *x*-ray. The coagulation time was much accelerated in most cases by medium and large doses. The leucocytes decreased.

Mikulicz-Radeki (Leipzig). Roentgen radiation and the rate of decrease of the blood-cells. The author found acceleration after operation, and subsequent to radiation a slowing, later an acceleration of the fall of the blood-cell count. His experience agreed with Risse's. He hopes to obtain prognostic information. The cause of the slowing is alteration of the fibrinogen or electric charging of the red cells.

Martius (Bonn). Experimental investigations upon radiation effect.

In general, one accepts the theory that the difference between the sensitivity of the carcinoma cells and that of the surrounding tissue is greater for hard rays than for soft. In experiments with the radiation of bean and pea seedlings Martius found more damage by the soft rays than by the hard, but caution should be observed in applying such results to man. At all events, it does not appear that an increase in the hardness of the ray is necessary in deep therapy. The hardness must be great enough so that absorption occurs at the desired depth.

Hofbauer (Dresden). Clinical observations on radiation of the hypophysis. Investigations on the effect of radiation of the midbrain and the hypophysis upon the female genital tract.

After radiation of the hypophysis in normal women, the uterus showed swelling. The question whether a functional stimulation of the uterus can be attained by radiation of the hypophysis was thus answered in the affirmative. Pains were elicited like those following injection of pituitary substance. Hypophyseal radiation in functional bleeding, for activating metabolism, is to be studied. In one case a loss of weight of 18 kg. was noted in fourteen days. After radiation of the hypophysis only, the following changes in carcinoma were demonstrated histologically: vacuolization of the protoplasm, cessation of mitosis, and the appearance of fibroblasts. The carcinoma was definitely "radium-ripe" (material from the Munich clinic). Even the most conservative interpretation finds that in the cases in which the hypophyseal radiation was of good effect, the tumor cells underwent a decrease of vitality, the connective tissue cells showed an inflammatory reaction and the resistance of the organism was increased. Roentgen or radium therapy was then used. In some cases there were frank failures.

Werner (Vienna). Experiences with radiation of the spleen in gynecology.

Werner has radiated the spleen in 74 cases of bleeding and had results in 70 per cent. The best results were in young girls and with inflammatory tumors of the adnexa. In the greater number of cases permanent effect was not attained. Direct influence of the substance governing coagulation was suggested. In placenta previa, no prophylactic effect was attained. Three cases of melena neonatorum were cured.

Vorländer (Freiburg). Histologic observations on radiated mice with and without carcinoma.

The author demonstrated, by the use of 900 white mice, the effect of radiation of carcinoma.

The end stage is the formation of a connective tissue capsule and fat tissue. The connective-tissue cellular reaction is what brings about the obliteration of all the carcinoma cells. Proliferation processes in the connective tissue are an expression of a general reaction.

Kok (Heidelberg). Experimental contribution to the radiation treatment of carcinoma.

After radiation of mouse carcinoma with 200 kv. through 0.5 mm. of copper Kok saw constant regression; never a stimulation of the tumors. Medium doses had better effect than large; the epilation dose is perhaps the best. Large fields were better than small. The same effect was produced when the opposite half of the mouse from the one containing the carcinoma was radiated. From these observations it follows that radiation therapy must be placed upon a different footing, and that colossal doses do harm.

Döderlein, Jr. (Munich). Critical investigation of the carcinoma question.

An agreement between histologic structure and clinical findings can be demonstrated, to the extent that no cured cases of adenocarcinoma were found. The healed cases were pure solid carcinomata, presumably derived from the superficial epithelium. "Atypical epithelial growths" are hardly to be differentiated histologically from true tumors.

Weibel (Vienna). The relation between pregnancy and uterine carcinoma. A special malignancy of carcinoma of the uterus in the gravid cannot be claimed. The author cites fifteen cases, all operable. In thirteen, the gravidity was evidently older than the carcinoma.

As to the relation between age and uterine carcinoma, old people showed no more recidives than the younger.

Discussion: Döderlein regards the problem of the hypophysis as interesting and worth consideration. The midbrain appears to dominate the endocrine system.

Geller (Breslau) in 1921 radiated 3 cases of dystrophia adiposogenitalis and gave 60 per cent of the single skin dose over the hypophysis; in two cases, no result. In acromegaly and with very weak menstruation he gave the full dose with improvement.

Hirsch (Altona) believes that by stimulation of the hypophysis the whole organism is made more fit. This can also be accomplished by the injection of endocrine preparations. He dissents from a direct influence of the radiation of the hypophysis on uterine carcinoma. The hypophysis presides over the ovary; when it is impaired, the ovary is impaired—temporary castration.

Werner (Heidelberg) has had no results from the treatment of bleeding by radiation of the hypophysis (as did Hofbauer). He has, however, obtained a good effect upon the pains of menstruation, and in amenorrhea has brought about the return of the menses.

Gragert (Greifswald) confirmed the decrease of the rate of fall of the blood count.

Vogt (Tübingen) has had results in only 50 per cent of the cases of bleeding treated by radiation of the spleen.

Teilhaber (Munich) agreed with Hofbauer upon the effect of ultraviolet rays and diathermy. Electromagnetic oscillations of various kinds stimulate connective-tissue formation.

Seitz (Frankfurt-on-Main) regards the local effect of the roentgen rays as more significant than the general effect, without deprecating the latter. The dose must destroy the function of the carcinoma cell. It is an error to place the general effect in the foreground, for thousands of carcinomata are healed by local radiation alone. It is necessary to produce a certain degree of swelling. The "carcinoma dose" given for the carcinoma of the cervix does not hold for carcinoma of the breast and other organs. The results of animal experiments and those of work on humans are not to be confused.

Wintz (Erlangen) is of the opinion that connective tissue replaces the carcinoma but does not choke it. The connective-tissue growth is secondary; the products of destruction of the carcinoma stimulate the connective tissue. He expects little from histologic investigations; a biologic reaction must be found, which indicates the reaction between the rays and a carcinoma. After radiation of the hypophysis he once observed dystrophia adiposogenitalis. When the hypophysis received 50 to 60 per cent of the single skin dose, eosinophilia was observed. The hypophysis is endangered by 90 per cent of the skin dose. Wintz admits the possibility of the sensitization of the carcinoma by radiating the hypophysis; which also, however, stimulates the body.

Kehrer (Dresden) holds the adenocarcinoma of the cervix as refractory to radiation. Radium has a better effect than the *x*-ray in carcinoma of the cervix. Radium does not injure the ovaries: the roentgen ray kills them. In old women he recommends ovarian transplantation.

Kraft (Dresden) has seen serous permeation of cutaneous carcinoma metastasis after radiation of the hypophysis. There is an effect on

the breast as in gravidity. He warns against large doses upon the brain, fearing late manifestations of harm.

Thies has seen more and larger multiple recidives after insufficient radiation than formerly. In respect to the results of radiation treatment, he notes that adnexa tumors may masquerade as inoperable carcinomata.

Lahm (Dresden) agrees with Wintz as to the theory of healing of carcinoma: first, disappearance of the carcinoma tissue, then invasion of the space by connective tissue. The principal consideration is to alter the degree of maturity of the carcinoma by the radiation. If eosinophile cells appear under the radiation treatment, the prognosis is doubly favorable. The preservation of the trophic nerves plays an important rôle. Lahm therefore does not use an excessively hard ray. A homogeneous deep field, however, must be had. Constitutional treatment is necessary to support the resistance of the body.

Holzbach (Mannheim). More than 80 per cent of the inoperable carcinomata of the uterus die from renal damage by growth of the carcinoma involving and compressing the ureters. He transplants the ureters into the vault of the bladder and prolongs life by preventing their being involved.

Hofbauer states that the ophthalmologists have never noted damage to the brain by radiation of the hypophysis.

Opitz (closing the discussion). Many examples are at hand to show the relation between the hypophysis and midbrain and the vegetative nervous system. Overdosing over the hypophysis is to be avoided. He does not recommend local radiation; he usually uses a combination of radium and roentgen rays.

Winter (Königsberg) Carcinoma statistics. The classification used hitherto: (1) Operable cases. (2) Borderline cases. (3) Inoperable. (4) Terminal. This is not useful. For comparative purposes and for clearing up the problem the statistics must deal with (1) the operable, and (2) the inoperable cases. Even if a few cases do show recidiv later, an observation period of five years suffices. It is false to construct statistics only upon the living; for many which have been counted as successful cases have already relapsed.

On the basis of a questionnaire sent to many university clinics and hospitals, Winter establishes the following cardinal requirements of carcinoma statistics:

1. All cases must be included which come to the clinic.
2. Division into operable (carcinoma limited to the uterus and its immediate vicinity) and inoperable (no kind of operation possible).
3. Enumeration of all fatal cases.
4. Observation period of *five* years.
5. No deductions allowed.
6. In the absolute percentage, all cases to be reckoned as relative percents of a given management.
7. Each author must differentiate, in the absolute number, between subjective and objective.

Discussion: Döderlein recommends a strict adherence to the cardinal principles. Statistics, to be worth anything, must include at least 300 cases. In the future perhaps large numbers of cases will allow statistics upon the result of elective treatments, when the one case is treated by operation, the other by radiation.

Opitz would add to the details mentioned by Winter, the local difference in malignancy of carcinoma. Thus Krönig had 38 per cent of cures in Jena, 5 per cent in Freiburg. Opitz also regards the division of cases into operable and in operable as too nice. The five-year observation limit is too short. Since we have been radiating carcinoma, the case has changed, and now it is not infrequent for recidiv to occur even after seven years. The most certain criterion is for the patient to remain well all her life.

Stoeckel (Ciel). Palpation is not sufficiently certain to form a basis of statistics. When rectoscopy and cystoscopy are more frequent, there will be better foundation than on palpation.

Von Jaschke (Ziessen) calls attention to the fact that there is an extraordinary difference in operation technique, and that the exact technique must be noted; not every Wertheim operation is a true Wertheim, but it may be reported as such. Krönig operated in Jena much more radically than he did later in Freiburg. This is the explanation for the difference in results mentioned by Opitz.

The presiding officer, Menge, spoke for improved statistics. The present statistics are made upon operative therapy; we paste the new onto the old. Our grandsons will laugh at our statistics because of the ridiculous classifications. Menge pleads for statistics according to length of life: after a certain treatment so and so many live two, three, four years, etc. To the number of the dead should be added the number that have disappeared from observation. Statement should be added as to whether the survivors are found, by palpation, to be free from recurrence.

At the conclusion, upon resolution of the society, the statistics worked out by Winter were accepted as the ones to be employed, perhaps in connection with others.

DANDY, WALTER E. Localizing brain tumors in comatose patients. *Surg., Gynec. & Obst.*, May, 1923, xxxvi, 641.

The author gives in full a detailed statement of his method and the indications for the determination of communication between the cerebral ventricles and the estimation of their position and size without the injection of air. Roughly estimated, not more than 50 per cent of all brain tumors are localizable by neurological and roentgenological examinations, and it is for the localization of the other half that cerebral pneumography is of the greatest value.

The emergency method proposed when cerebral pneumography is not possible is to estimate the size, position, and intercommunication of the ventricles by aspiration of the fluid in the lateral ventricles (and at times from the cisterna magna). Puncture of both ventricles is always necessary.

The article is abundantly illustrated by drawings, photographs and roentgenograms.

The author expresses the hope that he may publish in detail a large series of brain tumors in which the use of cerebral pneumography has been the means of localizing the growth.

GUISEZ, J. Radium treatment of cancer of the esophagus. *Presse méd.*, Feb. 28, 1923, xxxi, 193.

Guisez since 1909 has treated 180 cases of cancer of the esophagus with radium rays. During the first few years the benefit was only palliative, but during the last three years a number of apparent cures have been realized. This improvement in results he believes depends upon improvement in technique. In all the cases treated during the last six months not a trace of cancer can be seen and all difficulty in swallowing has disappeared. The endoscopic pictures of a number of cases are reproduced and complete details of treatment and dosage are included in the text.

RIEDER. Irradiation sickness. *Strahlentherapie*, xii, p. 573.

The general manifestations of irradiation sickness ("Roentgen Kater" of the Germans) can be diminished by means of thorough ventilation of the radiation room. As the author considers the electrical charging of the patient as one of the causes of after-sickness, he recommends that the electricity be grounded through a cable applied at the thigh and connected with the water conduction. Great caution is needed on account of the danger of short-circuiting. The grounding is preferably employed only with a minimum distance of 40 cm. between the focus and the skin. Unnecessarily large fields should also be avoided. The radiated body-space should be restricted to the smallest possible measure. By means of administration of laudanum-scopolamin, it is possible to reduce the general manifestations to a minimum degree, also in radiations of the splanchnic region where there is a special tendency to after-sickness.

LOTSY. A case of left-sided renal stone together with gall-stones in the colon. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1923, xxx, 214.

A native Egyptian was referred to the author in Cairo for examination of the left kidney. A shadow of a large renal stone was found, and there were also several shadows lower in the abdomen which changed their position readily. A history of severe epigastric cramps three or four weeks before, followed by jaundice, was then elicited. Lotsy concluded that the shadows in question were due to gall-stones which had lain meanwhile in the cecum, but had been mobilized by the castor-oil taken the night before examination. He gave the patient a physic and directed him to wash all stools through a sieve. However, the patient was not very bright and on his return he said that he had found nothing. Reexamination showed that the shadows in question had disappeared, though the renal stone shadow was still there. Lotsy compares the shadows to those shown by Carman in his text (2d edition) in Figures 355, 358, 359 and 361.

KLEINBERG, S. Periosteal chondrosarcoma. *Internat. Clin.*, 1923, ii, 33d series, 247.

The patient, a man nineteen years old, was well until he suffered slight trauma to the knee two months before he was seen by Kleinberg on December 9, 1922. The writer therefore regards the sarcoma as due to the trauma, which consisted of striking the knee against a ladder. As this injury occurred while the man was at work, there arises the question of compensability under the laws of New York.

A small shadow of bone density, shown by oxygen inflation of the joint to be continuous with the patella, diverted the attention of the roentgenologist and all the examining physicians away from the area of density in the head of the tibia that bespoke the tumor. Kleinberg diagnosed osteomyelitis or neoplasm from the films the patient brought with him, and on December 12, evacuated a deposit of gray friable tissue, underlaid by eroded dense bone, some of which was removed. The slides of the tissue, which was very cellular with but little stroma, were examined later by Dr. James Ewing, whose diagnosis was periosteal chondro-

sarcoma. The dense shadow in the patellar region, out of the tumor zone, was found due to cartilage.

A mid-thigh amputation was performed on December 21, 1922, and as late as July 14 of the present year (personal communication to the abstractor from Dr. Kleinberg) the patient was free from evidence of local or metastatic recurrence. When first seen he was pale and thin. He now weighs several pounds more than before the amputation, and appears to be entirely well.

SCHREUS. Studies on static electricity of the roentgen tube. *Fortschr. a. d. Geb. d. Rontgenstrablen*, xxviii, Hft. 2.

Besides the gliding sparks which pass on the outer wall of the tube from the anticathode to the cathode, there are the cathode neck-sparks, which originate at the cathode and terminate in the insertion of the cathode neck at the tube-sphere. These sparks give a strong light and are accompanied by a loud crackling sound. The danger of penetration may be prevented by lengthening the cathode-neck. At the same time, the author carried out investigations concerning the distribution of the charge in the tube in general. For details, the reader is referred to the original article.

SABERTON. Ante-operative *x*-ray irradiation. *Arch. Radiol. & Electrotb.*, Aug., 1922, p. 91.

In discussing a paper on the employment of deep radiotherapy by several French authors, Saberton stated that the time has not yet come when we can feel justified in advising our patients with an early operable growth to have radiation treatment rather than operation. In favor of ante-operative radiation we have the fact that the patient is in a better state of health to stand massive dosage than would be the case after an operation, and also there is less risk of a surgeon spreading active cancer cells about the body by the surgical trauma he has to carry out. Against ante-operative radiation we have the fact that a patient ought to wait for four to six weeks after a massive radiation before an operation is undertaken. In many cases, both ante and post, radiation treatments in conjunction with burying emanation needles at the time of operation will have to be carried out.

The question of dosage and the advantages and disadvantages of small and large radiation fields must be carefully considered in each individual case, and a line of treatment adopted to suit the particular case we have in hand. The theory of an antitoxin being formed as a result of nature's efforts to cure the disease is a fascinating one.

HIRSCH. Experiences with the Loose filter. *Strablentherapie*, xii, 560.

Loose attributes his unparalleled success to the employment of a crystal filter utilized by him, the exact composition of which is not stated. Hirsch worked with this filter, which, in his opinion, corresponds with respect to its power of absorption to an aluminum filter of about 6 mm. thickness. The biological effects, as was to have been anticipated, differed in no way from those of ordinary filtration. Sensitive tumors subsided, whereas obstinate tumors proved refractory.

DAVIS, GEORGE G. Osteosclerosis fragilis generalisata. *J. Exper. M.*, Mar. 1, 1923, xxxvii, No. 3, p. 449.

Albers-Schönberg's disease, or marble bone, is a rare condition characterized by a pathological fracture following a rather trivial injury, the fracture occurring as the result of a rather obscure bone condition termed osteosclerosis fragilis generalisata. Only 9 other cases of this disease have been reported, all in foreign literature.

An *x*-ray summary of the literature is appended to the report of the case. The article constitutes a very important contribution to roentgen literature.

KOTHEN. The measure of the percentage depth dose with Kienböch strips after the method of Baumeister. *Fortschr. a. d. Geb. d. Röntgenstrablen*, xxviii, Hft. 2.

From his experiments, the author draws the conclusion that with hard rays, such as are employed for the treatment of carcinoma, the Baumeister procedure is insufficient because it leads to overdosage. Also in the scope of softer rays, there still remains the difficulty of accurate registration, so that this procedure can be regarded only as an emergency measure, until the iontoquantimeter becomes so well equipped that it can serve as a general adjunct of practical roentgenology, due to its convenient manipulation and reasonable price.

PORTMANN, U. V. The efficiency of radiation therapy. *J. Lab. & Clin. M.*, Aug., 1923, viii, 716.

The author concludes that in order to obtain the best results in the treatment of malignant diseases by radiation the physical principles of the production and action of the *x*-rays and of radium must be understood.

It is usually impossible to deliver a therapeutic dose of *x*-ray radiation to deeply situated areas. The large deep doses which were first reported are not obtainable under present practical working conditions.

Radiation by either the *x*-rays or radium alone is insufficient; they should be used in proper combination.

The danger of insufficient radiation is as great or greater than that of overradiation; the desideratum is the administration of the proper dose at the first treatment.

DRÜNER, L. The technique of fluoroscopy: description of a new appliance. *Deutsche Ztschr. f. Chir.*, July, 1921, clxv, 275.

Fluoroscopic technique is threatened with the danger of becoming dependent upon large, expensive, stationary apparatus, which interferes with the movements of the surgeon, and moreover, does not entirely meet operative requirements. Drüner describes a simple appliance, manufactured by the hospital carpenters and engineer, destined for roentgenoscopic operations. The usefulness of this appliance is illustrated by four case histories. The outfit consists of three small exchangeable tables, under which the entire roentgen apparatus is lodged. The sequence of the tables may be changed according to requirements. I. Board and interruptor; II. Induction; III. Tube on a slide. The table bearing the tube is always placed under that portion of the body which is to be operated upon. The small apparatus comes from the factory of Siemens and Halske. Conduction from each plug with 6 ampere and 110 volt continued current. The essential feature is the full utilization of even a small outfit. It is most important for the appliance to permit the adjustment of all positions which are indispensable for the surgeon, such as the breech and back position, the breech-abdominal position, and elevation of the pelvis.

HIRSCH, HENRI. Concerning roentgen sickness and roentgen cachexia. *Deutsche med. Wchnschr.*, Dec. 8, 1922, p. 1646.

The author points out that the so-called Roentgen Kater (*x*-ray morning after sickness) and roentgen cachexia are manifestations of one identical injury, in the sense that a reparable damage of the endocrinic apparatus leads to the transitory phenomena of *x*-ray sickness, whereas an irreparable damage of the internal secretory system finds its expression in chronic cachectic conditions. Roentgen "sickness" is an acute manifestation, which originates after the application of definite *x*-ray doses, in excess of a certain limit, and is essentially dependent in its degree on purely individual fluctuations corresponding to the constitutional diathesis of the radiated individual. This acute condition subsides sooner or later, according to the patient's constitution, but may persist up to six weeks in variable intensity. The blood picture after intensive radiations shows at first, a slight leucocytosis, which, later on, passes into leucopenia; the lymphocytes gradually increase at first after the radiation and then diminish very considerably. The blood picture gradually recovers, and at the end of about four to six weeks, the patient presents a normal blood formula, besides the physical recovery, in favorable cases. Otherwise, the condition passes into the picture of cachexia, which here must be referred to a permanent damage of the endocrinic system through the action of the roentgen rays.

BARTRAM, GERHARD. Localization of the portio vaginalis in gynecological deep therapy. *München. med. Wchnschr.*, Feb. 9, 1923, p. 178.

For the accurate localization of the object of radiation, so that the central ray may reach its middle—an essential requirement, especially in the radiation of malignant tumors—the author has constructed a simple "directing circle," based on the ordinary circle used for pelvic measurements. This small instrument may serve for the determination of abdominal, dorsal, and also vulvar fields. Although it is planned primarily as an adjuvant in the radiation of carcinoma of the portio, its employment permits an essentially more accurate dosage also in radiations of the uterine fundus and ovaries than is possible by means of a mere estimate of the position of these organs. Its usefulness in carcinoma of the rectum is very evident.

MINET, H. Calcified hydatid cysts of the kidney. *J. d'urol. méd. et chir.*, 12, p. 13.

Description of a calcified hydatid cyst, which had developed in the lower pole of a calculous kidney. The roentgenogram showed, aside from two shadows of calculi, a large rounded mottled shadow with local lighter spots, corresponding to the irregular distribution of the calcium deposits within the cyst.

WETTERER. Roentgen treatment of the complications of gonorrhea. *Strahlentherapie*, xii, 469.

In numerous complications of gonorrhea, Wetterer had very excellent results with *x*-ray radiation. In gonococcal arthritis, the radiations should be instituted as promptly as possible. Equally good results were obtained in all joints. The monoarticular and the polyarticular cases have an equally favorable prognosis. Cases of periostitis are also well adapted to this treatment, especially in the early edematous stage. There was no failure among 75 cases of gonococcal disease of the organs of motion. The radiations are applied with highly filtered rays. The dose remains below the erythema limit. The many other

complications of gonorrhea, in which good results may be obtained with *x*-rays, are of less surgical interest.

KÖNIG, FRITZ. Operation in an irradiated field. *Med. Klin.*, 1921, No. 43.

The author has noted that after slight and more extensive operations in regions that have been previously treated with the roentgen rays, the wound has not healed normally; necrosis has occurred, sometimes even suppurative breaking down of tissue; but after a period, the necrotic material was cast off and normal granulation took place. The author believes that after intensive roentgen radiation there is a latent weakness in the irradiated tissue, varying according to individual predisposition, which does not become manifest unless some special provocation, such as operation, leads to necrosis.

HOLZKNECHT. Dosage in deep roentgen therapy from the biological point of view. *Vox med.*, 1921, iii, No. 3.

Where it is necessary to destroy tissues, as in carcinoma and most malignant tumors, a single large dose of the roentgen rays is indicated. In tuberculosis, on the other hand, experience has shown that repeated small doses are more effective. It is not necessary to destroy, but rather to strengthen the resistance of the organism. In the more severe types of tuberculosis, the dosage should be very carefully adjusted. In irradiating glands with inner secretions, their function should be disturbed as little as possible. The dosage should be carefully adjusted in each case by beginning with small and medium doses, and observing results.

JÜNGLING, OTTO. Roentgen treatment of surgical tuberculosis. *Med. Cor.-Bl. d. württemb. ärtzl. Landesver.*, xci, Nos. 38 and 40.

Roentgen rays are not a specific in the treatment of tuberculosis. They do not directly injure the tubercle bacilli, nor do they destroy the tubercles. The epithelioid cells as derivatives of connective tissue are very resistant to the rays. The higher doses do not improve the results; on the contrary, small doses (20 to 50 per cent of the skin erythema dose) are more effective than larger doses. Apparently, the rays act upon the lymphocytic elements of the tubercle, which are very radiosensitive, and are destroyed by the smallest doses. With tuberculous lymph glands, roentgen-ray treatment is the method of choice; general constitutional treatment for tuberculosis should be combined with the local treatment. Results with tuberculous peritonitis are also good. In unilateral tuberculosis of the kidneys, as well as in unilateral tuberculosis of the epididymis, operation is indicated, in order to prevent the spread of the infection. Postoperative ureteral fistulae respond readily to the roentgen ray: bladder tuberculosis, less well. In bone and joint tuberculosis all sequestra should be surgically removed. Iselin thinks that on technical grounds, greatly enlarged joints should not be *x*-rayed; the author, however, has found *x*-ray treatments suitable in certain cases of this type.

The method ensures a fairly accurate dosage, permits the working-out of the optimum dose and a comparison between the results of different therapeutists, and prevents late roentgen injuries, which is of special importance.

SPINELLI, M. Contribution to the roentgen and radium treatment of uterine cancer. *Actinoterapia*, 1921, ii, No. 3.

The author reports early results in radium-roentgen treatment of uterine cancer. Clinical cure was obtained; in precancerous stages in 100 per cent (18 cases), in corpus carcinoma in 87 per cent (of a total of 8 cases), in diffuse cervix carcinoma on the borderline of operability in 75 per cent (of 9 cases), in operable carcinoma or recurrences in 48 per cent (of a total of 56 cases). Radium treatment alone was used in the precancerous stage, but radium treatment (4,000 to 10,000 mg. hrs.) combined with intensive roentgen-ray treatment, using seven fields, in all other cases.

GROEDEL. Encapsulated pleura as seen roentgenologically. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 2.

The author describes the roentgen-ray appearances of encysted pleurisies, which vary according to their site. Case reports and roentgenograms are presented with the pleural exudate above the right upper lobe, with interlobular pleurisy, traumatic exudative pleurisy, locular pleural exudates, and exudative mediastinal pleurisy, and the difference between these conditions and other similar pathological conditions is illustrated and explained (abscesses, echinococcus cysts, hematoma, etc.) Some of these conditions have not been demonstrated elsewhere. Early roentgenological diagnosis may often save life.

HAMMER. Roentgen treatment of scleroderma. *Münchn. med. Wchnschr.*, 1921, No. 35, p. 1109.

The author has observed marked improvement in many cases of scleroderma after roentgen-ray treatment of the thyroid and thymus. This was especially true of cases with goiter and symptoms of thyrotoxicosis. Technique: 30–35 cm. spark distance, 170–180 kv., 2 ma., *heavy metal* filters, about ⅕ skin erythema dose, every two to four weeks.

WILLE, O. The value of the tube beneath the table in deep roentgen therapy. *Münchcn. med. Wchnschr.*, 1921, p. 1254.

For the treatment of large fields, the author has adjusted a tube fixed under the *x*-ray table for therapeutic purposes. In this way two fields can be treated simultaneously. With slender Coolidge tubes, the apparatus is easy to adjust. This arrangement is of special value if used with the Dessauer-Warnekros apparatus. The entire arrangement is shown in an illustration.

RZEWUSKI. Osmo regulation of roentgen tubes. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 3.

The author reports on his experiments with hardening roentgen-ray tubes that are too weak. The method was described by the English writer Kaye as early as 1898. If the regulating palladium tube is heated only with the point, that is, the oxidizing portion of the flame to glowing heat, then the hydrogen in the tube is burned and the tube becomes harder. Heating to 200° is sufficient. The author treated over-regenerated tubes that he wished to save with the palladium regulating tubes.

RAMOND, F., JACQUELIN, CH., and BORRIEN. Gastric spasms. *Presse méd.*, July 20, 1921, lviii.

According to the anatomical conditions demonstrated, there are three types of gastric cramps—due to cardiospasm, gastrospasm (involving the region of the fundus) and pylorospasm. The Braun or Gubaroff valve which some authors believe to be present at the cardia as a cause of spasm and aerophagy is found only very rarely at autopsy. On the other hand, there is in many cases a mechanical cause for cardiospasm in that the abdominal portion of the esophagus is abnormally kinked. The functional symptoms of cardiospasm are slight; occasional local pain, sometimes a painful pressure point over the ensiform process, a feeling of fulness after eating, no dysphagia. The roentgenogram is typical, showing dilatation of the esophagus, and a wide bismuth column, broken up by air spaces which pass slowly along the gastric walls in the stomach, although the pressure of the hypertrophied esophageal musculature is sufficient to push this column forward and overcome the obstruction at the cardia.

Gastrospasm, which is usually combined with pylorospasm, is occasionally observed alone, chiefly in acute gastritis, also in ulcer of the lesser curvature, and in duodenal ulcer, in cholelithiasis, renal stone, and appendicitis, and in neuropaths. Gastrospasm alone causes no subjective symptoms and is shown only by roentgenological examination (increased peristalsis, hour-glass stomach). On the other hand, gastrospasm combined with pylorospasm causes symptoms of pylorospasm and pyloric stenosis, cramp-like pains, feeling of fulness, regurgitation of air and food contents, excess or absence of peristalsis, so that the stomach appears fixed "in systole." In pylorospasm alone the subjective and objective symptoms are the same. In the roentgenological examination, the bismuth meal has a soothing effect, and hence slight spasms are often not visualized. The roentgenogram shows that only a small part of the gastric content passes into the duodenum and there remains unchanged, although the stomach may show peristalsis. Brugel's symptom is also evidence of pylorospasm. The administration of suprarenin (0.5 gm.) increased the spasm: atropin diminishes it. Therapeutically, in addition to the determination of the underlying cause and the corresponding dietetic treatment, belladonna is chiefly indicated, also benzyl benzoate, morphin and opium are less valuable.

KNOX, R. Treatment by *x*-ray and radium. *Edinb. M. J.*, New Ser., May, 1921, xxvi, No. 5.

In roentgen and radium therapy, the decisive factor is the wave-length, so that rays of different wave-lengths must always be available for the various requirements. All discussions as to the greater or less value of *x*-ray as compared to radium are therefore useless, the essential point being that with available apparatus, no short-wave rays can be produced, corresponding to the gamma rays of radium. The utilization of radium and roentgen apparatus seems to be the most rational procedure. Superficial lesions are most favorably influenced, and there is in addition the advantage of direct observation. It must be kept in mind, however, that certain malignant formations, such as rodent ulcer and epitheliomata, may prove rebellious against all radiation therapy. Overdosage is cautioned against in alopecia areata, where the *x*-rays are always efficient. In rodent ulcer, the frequent recurrences after simple roentgen radiation are noteworthy, whereas radium radiation yields more durable cures. In lupus, radiation with radium, roentgen and violet rays is justified, but special precautions are needed on account of the damage to the skin due to the disease. The same remark is true for acne, where vaccination and medicinal therapy may also be successfully employed. Hyperidrosis is favorably modified by *x*-rays. Blood diseases associated with enlargement of the spleen are temporarily improved by *x*-rays in the same way as through splenectomy, which likewise

yields no permanent cures. In exophthalmic goiter, long-continued roentgen radiation together with rest and medicinal therapy may be equally as successful as operative treatment. Inflamed and enlarged glands are rapidly reduced in size through roentgen radiation, also lymphadenomata and sarcomatous glands, although recurrences rapidly occur in the latter, which finally cease to react to the radiation. Tuberculous glands diminish slowly in size, and rarely disappear entirely, often showing a tendency to recurrence, so that the removal of the reduced glands is recommended. Carcinomatous glands are hardly affected by radiation as a rule. Uterine myomata are favorably influenced in a general way with respect to reduction in size, and even more so with respect to hemorrhage. In malignant tumors, preliminary radiation before the operation enters into consideration; furthermore, postoperative radiation, radiation of recurrences and ray treatment of inoperable cases. Preliminary radiation is recommended in all cases when the operation is not essentially delayed by the radiation. Preceding the radical operation for mammary cancer, radiation seems to be especially valuable, as the lymph glands are modified by the radiation, and epilation of the axilla is produced. Also postoperative radiation enters primarily into consideration for mammary carcinomata. Radiation treatment should be instituted promptly and carried out systematically. The same is true for recurrent and inoperable tumors, in which the collaboration of the practitioner, the surgeon and the roentgenologist may be expected to furnish good results.

GLOVER, DONALD M. Osteopsathyrosis: Report of a case. *Arch. Surg.*, Nov., 1922, v, 464.

The author reports a new case of osteopsathyrosis with roentgenograms of 11 different fractures in the same patient occurring between the age of nine months and his death at seven and a half years. A brief summary of the literature is recorded. Excellent roentgenograms accompany the article, which discusses not only the history of this patient but also terminology, classification of cases, etiology and pathology. As to symptomatology, there are no constant symptoms other than the tendency toward frequent fractures. In some of the earlier cases the appearance of the patients conforms more or less to type. They have a relatively large head, small chest and a protuberant abdomen. The later cases, however, may show no recognizable peculiarities of form.

The roentgen-ray findings have been summed up by Locke as follows:

"(1) A high degree of osteoporosis uniformly affected the entire skeleton, the variations in density giving a mottled appearance; (2) marked deformities of the long bones of the extremities, usually of the angular type, due to fractures, rarely also some actual bowing; (3) apparently normal size and shape of bones, except as altered by fractures and resulting callous formation; (4) often excess callous formation with variable degree of calcification. A transverse line of decalcification is often seen at the point of previous fracture; (5) the epiphyseal line is straight, cartilage is always thin; (6) a very faint shadow is given by all the bones, frequently scarcely more dense than that of the surrounding soft parts; (7) the cortex is thin, irregular and deficient in salts; (8) the spongiosa of both epiphysis and diaphysis is extremely faint with entire absence of normal markings; (9) the medullary cavity is very irregular in outline and dilated." These changes are considerably less marked in some of the milder cases, such as the one described in this article.

Metabolism studies have suggested that calcium metabolism may have some bearing on this type of bone fragility as well as on the deformities of rickets.

The outlook in cases of osteopsathyrosis is poor, in spite of the fact that a few patients have grown to adult life, apparently overcoming the bone fragility from which they suffered in earlier years. Most of the patients that survive are deformed by earlier fractures. Few fractures occur after the patient is in the early twenties, and after that time the prognosis is fairly good. Below that age, however, the mortality is high. The mortality is almost 100 per cent in the fetal type, the majority dying in utero.

The diagnosis is usually perfectly clear, because there is no other congenital disease in which multiple fractures occur. Rickets and syphilis occasionally cause fractures in young children; but rarely more than two or three fractures occur in the same person as a result of these affections.

WEIS, HOWARD A. A contribution to the study of the effects of radium upon rabbit ovaries. *Surg., Gynec., & Obst.*, Mar., 1923, xxxvi, 373.

In the experimental work the dosage of radium used was always 600 mgm. hours, that dosage being selected because it is conceded by most authorities that 600 mgm. hours of radium applied intrauterinely will be usually sufficient to produce an amenorrhea for several months, and sometimes permanently; the generally accepted theory being that this

result is due to the fact that the radium rays destroy all the maturing follicles most advanced in development, the return of menstruation occurring because the more immature follicles had not been destroyed. When these matured, menstruation resulted. But this explanation is contrary to the biological law which states that the less mature the cell, the greater its susceptibility to disintegrating influences.

For most of the exposures 50 mgm. of radium was employed in the form of radium barium sulphate in two 25-mgm. tubes, filtered with a glass, a silver and a brass screen, and this inserted in a rubber tube of 1 mm. thickness. The tubes were then fastened to a lead frame by adhesive, and this fastened by adhesive and a wide gauze bandage, as nearly over the rabbit's ovary as could be determined. The dose was 600 mgm. hours.

The complete details of the treatment are given in the body of the article. The author found that in none of the ovaries was there any change in the single row of germinal epithelium after exposure to radium and no evidence of any obliterative endarteritis. Six ovaries showed little or no change evident in the connective tissue cortex; but ten others showed an increase in the number of cells in this area, and four showed a definite widening of this zone. Certainly the author found that the young and early maturing ova had not been damaged. Thus the author did not feel justified in concluding that 600 mgm. hours of radium had any ultimate detrimental effect upon rabbit ovaries.

The author ventures the opinion that when radium is given intrauterinely for a case of menorrhagia, for example, the resulting amenorrhea is not due to the effect of the radium upon the ovarian follicles, but to the effect upon the endometrium which receives a severe burn from the radium. If the burn be extensive enough a permanent amenorrhea results; and if not so severe, the amenorrhea persists for only a few months.

The above views constitute a definite departure from the accepted theories of the effect of radium.

Schmidt, Ernst Albert. Experimental and histological investigations concerning the effect of roentgen rays upon the staining properties of tissue. *Strablentherapie*, xii, 517.

Radiated and unradiated mice were stained with trypan-blue while living; two days after the last injection, one stained animal and one control animal were killed. Microscopic examinations were made of the skin, mucosa, liver, spleen, testicles or ovaries, respectively, heart and muscles, brain, bone-marrow and blood. The radiated animals took the blue stain more rapidly and intensively. The organs were stained to a very variable degree of intensity. Details concerning the findings in the organs must be looked up in the original. The staining was expressed as a granular staining and as diffuse protoplasmic staining. The various organs showed differences with respect to the intensity of the coloration, with respect to the intracellular distribution of the pigment and with respect to the distribution of the color among the individual kinds of cells. In a series of experiments, a different behavior with respect to the above-mentioned points was noted in radiated as compared with unradiated animals, without its being possible to establish any deviation from the normal standard anatomo-histologically, by means of the customary post-mortem staining methods. The different behavior is regarded by the author as a change of cellular function, the various modifications being interpreted by him as follows: Increased accumulation of pigments in the form of granules is considered as an increased function; diffuse coloration of the protoplasm, as a slight damage; nuclear staining as a post-mortem phenomenon and as the expression of a grave cellular lesion. In view of the fact that all these differences in staining take place in the connective tissue, this must be considered to play an important part in the action of the rays. Vital staining, according to these findings, appears to be a valuable adjuvant for the representation of slight cellular changes of functional character.

Voorhoeve, N. The roentgenologic symptom-complex of horseshoe kidney. *Fortschr. a. d. Geb. d. Röentgenstrahlen*, 1923, xxx, 201.

In the *Nederl. Tijdschr. v. Geneesk.*, 1916, ii, 1250, Voorhoeve has told how he diagnosed horseshoe kidney in a patient seen in Amsterdam in 1915. In 1919 he saw a second patient in whom he succeeded in making this diagnosis. Both patients came to operation for removal of a demonstrated stone. In the first case the connecting bridge had not been visualized, and operation showed it to be a narrow fibrous strand. In the second case it was partially visualized, and operation showed it to be large and thick.

The diagnosis therefore depends not necessarily upon visualization of the bridge, but on alterations of position and mobility of the kidneys due to its presence: (1) The median border of the kidneys parallels the vertebral column, or makes a much diminished angle with it, and (2) is closer to it than normally. (3) There is bilateral renal ptosis, which may be very marked. (4) The kidneys make no

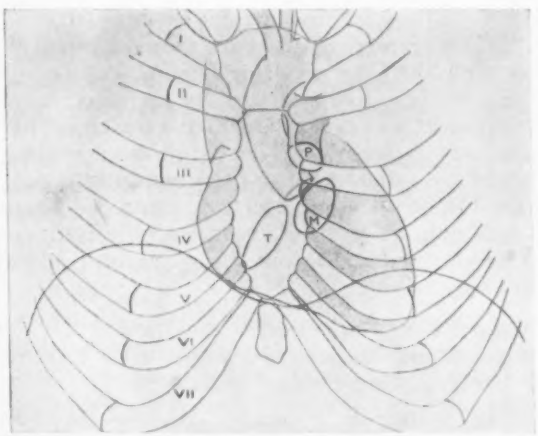
lateral excursion on respiration. In the author's first case, the vertical mobility was preserved, but this is not usual. (5) The lower pole can be demonstrated as ventral to the vertebral column. For this, the comparison of paired exposures in the ventrodorsal and the dorsoventral positions is of value.

In the absence of vertical mobility, not even the added aid of pyelography will always differentiate from a pair of congenitally dystopic kidneys that adhere to their surroundings. However, an equality of the ptosis makes horseshoe kidney the more probable.

The author refers to reports of a case of Quartero's and one of van Hasselt's in which his method established the diagnosis, and to a report by de Groot of the agreement of findings in the examination of a patient in whom operation had already demonstrated the presence of a horseshoe kidney. He emphasizes that the method will diagnose the condition even when it has not been suspected.

LeWald, Leon T. The relation of the heart, pericardium and the heart valves to the anterior chest wall. *Arch. Surg.*, Jan., 1923, vi, 89.

The author calls attention to the inaccurate older methods of locating the valves of the heart by dissection, and then describes a



Outline drawing of teleoroentgenogram and stereoscopic roentgenograms. The position of the valves T (tricuspic), M (mitral) and P (pulmonary) may be noted. The aortic valve is indicated by the beginning of the aorta.

method of localization by means of teleoroentgenography in a cadaver in which wires had been placed in the valve orifices by Dr. H. D. Senior, Professor of Anatomy at Bellevue Medical College.

The frozen thorax was cut accurately, by means of a band saw, in the frontal plane so as to open both auricles from behind, without interfering with the contour of the heart. In the intact interior portion of the thorax, the mitral and tricuspid valves were readily accessible. Wires were bent so as to fit accurately the groove corresponding to the attachment of the valves to the heart wall. The wires were placed in position from the auricle, and in the case of the tricuspid valve, fixed by means of two sutures. The cusps of both auriculoventricular valves were found to be in apposition. The interior of the aorta was reached through the anterior wall of the left auricle. The region of the pulmonary valve was made accessible by removing the remainder of the left lung and cutting the artery longitudinally from the left side. Wires were shaped to fit the aortic and pulmonary orifices and placed so that they were in contact with the deepest part of each of the semilunar valve cusps, which provided excellent guides in placing the wires. After placing the pulmonary ring, the cut edges of the vessel came into position. The accuracy of the position of the wires was verified after roentgenograms had been taken.

The apex is in the fifth intercostal space, from 7.5 to 8 cm. (3 to 3¼ in.) from the median line. The base corresponds to an imaginary line drawn from a point 1 cm. (⅖ in.) below the second left chondrosternal articulation, and 3 cm. (1⅕ in.) from the median line to another point the same distance from the median line, 1 cm. above the right chondrosternal articulation. The margo acutus, or lower border, corresponds to a line drawn from the apex through the xiphisternal articulation to a point on the sixth costal cartilage, 2 cm. to the right of the median line. The right border of the heart may be indicated approximately by an imaginary line (slightly convex to right), joining the right ends of the first and second lines. The left border corresponds to a line (slightly convex to left) joining the left end of the first line to the apex.

If a line is drawn from the upper margin of the left third chondrosternal articulation to the right edge of the sternum in the fifth intercostal space, the upper end of the line will lie over the center of the pulmonary orifice, and the lower two thirds of it (approximately) will overlie the main axis of the tricuspid orifice. The aortic orifice is immediately to the left of the above line, with its center at the left edge of the sternum, opposite the third space. The mitral orifice is very largely behind the third left interspace; its upper end is behind the third cartilage, its lower end behind the left margin of the sternum, opposite the fourth cartilage and space.

LeWald, Leon T., and Green, Nathan W. The differential diagnosis between tuberculosis and lung abscess. *Arch. Surg.*, Jan., 1923, vi, 303.

The authors record a group of 8 cases of abscess of the lung successfully operated upon. The cases are classified as follows: (1) bronchiectasis; (2) bronchiectatic abscess; (3) suppurative pneumonitis; (4) extrabronchial abscess.

Several of the cases had histories which had led to an erroneous presumption of pulmonary tuberculosis, largely because of the presence of blood in the sputum, persistent cough and loss of weight. The authors call attention to the accuracy of the roentgenographic diagnosis of abscess of the lung and its differentiation from tuberculosis when properly interpreted. The attention is also called to the fact that the sputum does not always have a fetid odor in abscess of the lung. Clubbing of the fingers is one of the most definite appearances. Repeated negative examination of the sputum for tubercle bacilli confirmed the diagnosis of lung abscess, in spite of the fact that three of the cases had been referred from tuberculosis clinics. The origin of the abscess in each case was of postpneumonic or postoperative nature; two cases followed tonsillectomy and one followed an operation on the gall-bladder.

Kaess, F. W. Temporary sterilization of the parotid by *x*-rays in the treatment of salivary fistulae. *Zentralbl. f. Chir.*, Jan. 6 and Apr. 21, 1923, pp. 14 and 641.

Parotid fistulae have occurred frequently since the World War, as a result of war wounds. Surgical treatment of these fistulae has not proved very satisfactory. Kaess reports 2 cases treated with *x*-rays. In the first case, bilateral parotid fistulae resulted from a gunshot wound; the fistula on the left side was cured by operation. Operation on the right side, however, was not successful, and saliva continued to flow out of the fistulous opening. One treatment with *x*-rays was given with the following dosage: 120 F., 24 cm. skin target distance and 3 mm. aluminum filter. Within a few days all flow of saliva had ceased, and in a month the fistula was entirely closed. In the second case, there was a parotid fistula on the left side due to an injury to the face from a shell splinter. The wound had healed except for the fistula, from which there was a constant flow of saliva that had caused eczema of the cheek. This case had been treated by Leriche's method of division of the auriculotemporal nerve; this had resulted in temporary diminution of the flow of saliva, which had, however, increased again. A single treatment with the *x*-rays was given with a higher dosage than in the previous case, 150 F., 25 cm. skin target distance and 3 mm. aluminum filter. The flow of saliva ceased in a week and the fistula closed in two weeks. A month after treatment, the patient reported that the eczema was entirely healed, and he no longer suffered from dryness of the mouth, which had been constant previous to the closing of the fistula.

This method of treating parotid fistulae has been very little used; the author finds only one previous reference to it in the available literature. He recommends it, however, not merely in the more persistent types of fistulae, but also as an adjuvant to any operative treatment, especially as it is simple and conservative.

Kaess notes that since his report, Fraenkel of Charlottenberg has told him that he (Fraenkel) discussed the roentgen-ray treatment of parotid fistulae to diminish the secretion, and thus aid the healing of the fistula, in his treatises on "Roentgen-ray treatment of war wounds" (*Strahlentherapie*, 1916, vii), and "Treatment of severe fractures with stimulative roentgen-ray doses" (*Med. Klin.*, 1915, No. 8).

Schaedel, H. Radiation as an aid in the operative treatment of parotid fistula. *Zentralbl. f. Chir.*, Apr. 21, 1923, p. 640.

Schaedel reports one case of parotid fistula on the right side, resulting from a war wound; the flow of saliva was always increased when the patient was eating. Operative treatment had not been successful. The fistula was entirely healed by a roentgen-ray treatment with 25 cm. skin target distance; 160 kv., 2 ma., 0.5 zinc, 1.0 aluminum filter. A year later, it could be demonstrated that the right parotid gland was functioning.

Nordentoft, Severin. New points in the treatment of uterine cancer with radium. *Ugesk. f. Laeger*, 1921, lxxxiii, 75.

The author in a lecture discusses modern viewpoints for the radiation of cancer of the uterus. Radium rays are preferable to the *x*-rays (investigations of Aurich in Vienna). Radium capsule, for the protection of rectum and bladder; 7 mm. gold filter, in front and behind. Butterfly shape of area for transverse incision. In order to avoid a rotation of the capsule, Nordentoft employs elliptic capsules. Radiation (once) for twenty-two and one-half hours. Fifty milligrams radium, respectively, is inserted into the cervix, and through incision internally at the tuberosity of the ischium towards the obturator foramen.

SCHWEITZER. Life expectancy after radioactive treatment of carcinoma of the cervix. *Strahlentherapie*, xii, p. 501.

Inoperable carcinomata: 32 per cent primary cases. Operable carcinomata: 75 per cent primary cases. In the inoperable cases, 4.9 per cent permanent cures were obtained. For the operable cases, the permanent cures (six to seven years) amounted to 25 per cent. The author recommends operation followed by combined radium and *x*-ray treatment. In cases which have not been radically operated upon, supplementary after-radiation is still fairly promising. So-called "preparatory" radiations before the operation are cautioned against, on account of the danger of damage to the tissues.

LAHMANN. Combined roentgen and sunshine treatment of granuloma. *München. med. Wchnschr.*, 1921, p. 1249.

In a case of rapidly growing malignant lymph granuloma, roentgen-ray treatment alone had no therapeutic effect. On the contrary, the blood picture and the clinical condition were worse after each radiation. After the institution of intensive light treatment, with sunlight or the Alpine light, the blood picture, the patient's general condition and the reaction of the roentgen rays were all improved. The tumors were rapidly reduced in size during a febrile reaction, so that after a four months' treatment, the patient seemed entirely normal. Since there has been no recurrence in two years, this case may be regarded as probably cured.

RYDGAARD, FRODE. Vaquez' disease cured by *x*-ray treatment. *Hospitalstidende*, 1921, lxiv, Nos. 24 and 25.

Report of a case of polyglobulia megalosplenica (Vaquez' disease) in a woman of thirty-seven years, cured by *x*-ray irradiation. The author considers splenectomy as contraindicated in Vaquez' polyglobulia without complications. When radiation of the spleen alone is not sufficient, it may be combined with radiation of the long shaft bones.

WEIL. A rare roentgen finding in a child's femur. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 2.

The author reports a type of ossification process in the head of the femur, apparently never described previously: "Above the unchanged epiphyseal line there was a relatively small nucleus of the femur head with good body structure and normal calcium content. This nuclear mass is surrounded by a crescent-shaped area deficient in calcium, which toward the joint showed a transition to a similar crescent-shaped ring with normal calcium content. This process was the same on both sides, and in new roentgenograms, half a year later, showed no change."

SGALITZER, M. Roentgen diagnosis of renal calculi. *Archiv. f. klin. Chir.*, 1921, cxvi, 231.

The article is based on clinical material of the Eiselsberg Clinic. The ventrodorsal roentgen-ray examination if used alone is insufficient for the demonstration of kidney calculi, except in the typical cases in which the stone represents the effusion of the kidney pelvis and calyx, since there is a possibility of confusion with opaque formations of other organs. For proper orientation, also, lateral roentgenograms are necessary. In a directly lateral roentgenogram, concretions in a normally situated kidney are concealed by the anterior part of the body of the twelfth dorsal or the first to second lumbar vertebrae, or even by the upper part of the third lumbar vertebra. In a frontal roentgenogram, renal calculi which project over on the normal kidney shadow in the ventrodorsal roentgenogram are clearly distinguished from other opaque shadows. Calculi in a ptosed kidney which does not return to its normal position with the patient lying down, are projected in a frontal roentgenogram directly in front of the ventral surface of the last lumbar vertebra. The simultaneous absence of the kidney shadow and the demonstration of kidney stone close to the lowest lumbar vertebra in the ventrodorsal roentgenogram, and of the stone directly in front of the anterior surface of the same vertebra in the frontal roentgenogram, indicate the presence of horse-shoe kidney with stone. The use of the two plates in the diagnosis of renal stone gives very definite information in regard to the number, position and shape of the calculi. The ureter filled with a contrast material can be demonstrated along its entire length in the direct frontal as well as in the oblique roentgenogram, and this makes it possible to visualize all the anomalies in its course, which is important not only in diagnosis but also as a guide to surgical treatment. Ureteral stone situated in the part of the ureter above the pelvic bones can be demonstrated in a lateral roentgenogram.

HAUPT and PINOFF. The value of long-distance irradiation in deep therapy. *Deutsche med. Wchnschr.*, 1921, No. 15.

The deep dosage is not improved by an increased distance between focus and skin, or by a large tube. Physical and physiological (chemical-biological) problems are here involved together.

FALTA and HÖGLER. Radium therapy as a treatment method in internal medicine. *Strahlentherapie*, xii, 217.

Rather remarkable results in erythrocythemia after radiation of the spleen and the bones are described. The radiation areas are divided into fields. The small tubes are allowed to remain on the individual fields from two to eighteen hours. Lymphogranulations and lymphosarcoma, as well as tuberculous lymphomas were greatly benefited. A bone sarcoma at the occiput was made to disappear entirely (histological examination); bursitis subsided, the pains were relieved; one case of trigeminal neuralgia was freed from pains. Of 9 cases of peritoneal tuberculosis, radiated with radium, 6 purely serous cases healed smoothly; the nodular forms failed to react. Investigations on the action of radium in exophthalmic goiter are not yet concluded. In one case, the circumference of the neck diminished 6 cm. within three weeks, the pulse diminishing from 130 to 140 to 80 to 90. The domain of indications for radium treatment cannot yet be outlined. The question arises: Can cases refractory to the *x*-rays, or those cases which have become refractory through frequent *x*-ray radiation, be influenced by radium? It seems noteworthy that the phenomena of "after sickness" (the so-called "Roentgen-Kater" of the Germans) practically never occurred under radium treatment.

DAVID, O., and HIRSCH, ARNOLD. Experimental studies on the adrenalin content of the suprarenals following roentgen irradiation. *Klin.-therap. Wchnschr.*, April 23, 1923, p. 790.

Many authors claim that it is possible to exert an inhibitory or stimulative action on the growth and formation of vegetable as well as animal cells, by means of roentgen radiation. It is of special interest to observe such effects of radiation upon the internally secreting glands. The suprarenals here rank among the first objects of experimentation, being especially suitable for this inquiry. The results of the experiments are divided principally into four groups: The first group of observers noted roentgen lesions of the suprarenal parenchyma; the second group believed they saw a distinct lowering of the blood picture after radiation of the suprarenals in hypertonic conditions; the third group was unable in variable observations to establish an arbitrary and absolutely reliable influence upon the blood pressure; whereas the fourth group found the sugar metabolism to be modified through radiation of the suprarenals. The literature accordingly, furnishes no unanimous views as to the possibility of roentgen stimulation of the suprarenals. This is explained by the fact that different results were invariably obtained with different doses, especially as there was no reliable index for estimating the suprarenal function, the blood pressure which is utilized as an index by numerous writers being absolutely useless as such. In the absence of a reaction, the investigators presumably did not reach the suprarenals with the rays, or only in part, while in changes of the sugar metabolism, side-effects upon the pancreas may have intervened.

One of the authors (David) has previously pointed out that on radiation of the isolated suprarenal body, a reliable index is supplied in the first place by the adrenalin contents of the radiated organ, while the other organ, in the second place, constituted a useful method of comparison, provided laboratory animals are selected which have physiologically the same adrenalin contents in both suprarenal bodies. In the performance of accurate experiments, the following four points must be steadily kept in mind:

1. The physiological adrenalin contents of the suprarenals of the examined animals species must be accurately known.

2. The ray-cone must strike the gland separately, so that side-effects upon other organs are excluded.

3. Exact measurements of the administered *x*-ray doses must be practicable.

4. It must be possible to express the results of the radiation in exact terms.

The normal adrenalin contents of the laboratory animals—rabbits, guinea-pigs, dogs—are known through the experiments of Batelli and Ornstein, whose results may still be regarded as correct, in spite of the antiquated procedure. The second condition is met by the operative exposure of one suprarenal body in the animal, and the third condition is met by exposing the administered amount of rays in skin erythema doses (SKE). In order to comply with the fourth request for exact values, preliminary experiments must be performed, ascertaining if the experimental procedure as such, without radiation, acts in any way upon the adrenal system, in the sense of a functional change. It was found that this is not the case, and the preserved suprarenal body never presented a change deviating from the normal standard, as a result of the intervention. For the quantitative determination of the adrenalin contents, Folin's procedure modified by Quantmeyer and Autenrieth was selected. The conditions for the radiations were always identical. Altogether, 40 laboratory animals were radiated, including the preliminary experiments. The doses were 100, 75, 50 and 25 per

cent of the skin erythema doses, applied through filters of ½ mm. zinc, 3, 2, and 1 mm. aluminum. The time between radiations and killing of the animals amounted to eight days in the majority of cases. In the following table, prepared from four tables of the principal experiments, the accomplished efforts are compiled, expressed in percentages:

Dose	Number of Experiments	Unchanged	Adrenalin Production	
			Diminished	Increased
1 SKE	7	..	86 per cent	14 per cent
¾ SKE	6	..	50 per cent	50 per cent
½ SKE	8	..	50 per cent	50 per cent
¼ SKE	11	..	.....	100 per cent

The findings serve to show the following:

1. The adrenal system is amenable to influences by the *x*-rays.

2. A distinctly weakened function is obtained through radiation with one skin erythema dose.

3. A functional increase is obtained through radiation with ¼ skin erythema dose.

LICHTENBERG, A. Visualization of ureteral fistula by the *x*-rays. *Ztschr. f. Urol. Chir.*, vii, Hft. 1–3.

For the accurate determination of the site of a ureteral fistula, an *x*-ray catheter with division into centimeters is inserted into the corresponding (empty) ureter, and a thin, flexible, well-greased shadow-producing sound is introduced by way of the fistula. The last-named procedure is often tedious and difficult. By means of a roentgenogram, the place at which the two catheters come in contact is brought into view. Through subtraction of the portion of the ureteral catheter projecting beyond the intersection from the length of the inserted ureteral sound, the distance of the fistulous orifice from the vesical opening of the ureter is obtained.

ANSCHÜTZ and HELLMANN. The value of post-operative irradiation following radical surgery on mammary carcinoma. *München. med. Wchnschr.*, 1921, p. 1005.

The authors compare this material with the publications of the Tubingen, Marburg, Breslau and Leipsic clinics. In order to obtain a still more accurate differentiation as to the gravity of the cases, the second group of Steintal is divided by them into three subdivisions: Carcinoma, not adherent, glands palpable or found at operation; carcinoma adherent to the skin or the pectoralis muscle, glands positive; carcinoma adherent to the skin and the pectoralis muscle, glands positive. The third group yields bad results. The results in the Kiel clinic were better after radiation following the operation than without after-radiation. The outcome is referred by the authors to their radiation-technique, by means of which they obtained at a depth of 1 cm. 60 to 65 per cent of the carcinoma dose, and at a depth of 2 to 3 cm., 30 to 40 per cent of the carcinoma dose. The intrinsically insufficient effect of these relatively small doses is evidently compensated and rendered perfect, because these doses are applied often, at regular intervals (every four weeks) and the radiation was extended beyond one year. The authors accordingly worked with so-called "drawn out" doses, with a successful outcome in the post-operative therapy of mammary carcinoma. According to their experiences, the authors feel justified in seeing the secret of success in the correct employment of the dosage.

SCHÜTZE. Roentgen investigation of the duodenum. *Berl. klin. Wchnschr.*, 1921, No. 33.

The author shows that the duodenum is freely accessible to examination by the *x*-rays, provided fluoroscopy is sufficiently prolonged, up to ten minutes or longer. A great variety of changes are met with, for example, loop formations of partly semicircular, partly circular type. Changes in the position of the duodenum often supply the cause of manifestation which led to the diagnosis of "nervous stomach."

HÜTTEN. Adhesions following thyroid irradiation. *München. med. Wchnschr.*, 1921, p. 983.

In consequence of the uniform findings in his experiments, the author assumes a positive connection between the radiation of goiters and the formation of adhesions, and he, therefore, rejects radiations until practicable conditions are provided under which these adhesions do not occur. In his microscopic investigations he was unable to discover any specific influence of the *x*-rays upon the goiter tissue.

FRAENKEL, MANFRED. The influence of scattered radiation on glands of internal secretion. *Deutsche med. Wchnschr.*, 1921, No. 9.

Cases of remarkably prompt, hardly-ever-previously-observed, favorable modification of sarcoma, carcinoma, and metastases, have been described by Lenk. The author (Fraenkel) believes that the effect was not due to the scattered radiation, but to an endocrinic glandular action. Stimulating rays produce increased amounts of secretion in these glands, these secretions existing as a growth-inhibitory influence upon the precarcinomatous cells. In fully developed cellular degeneration, rapid destruction and absorption are induced, whereas even the maximum doses of the hardest rays are only capable of inhibiting develop-

ment. The objective is not a direct, cancer-destroying effect, but a reinforcement of the defensive mechanisms. This new radiation treatment of cancer offers the following advantages: The long sessions of several hours' duration are avoided; the neighboring tissue, whose intactness is very necessary, is not injured; and the cancer cachexia is not increased.

SCHINZ. The advantage of the roentgen examination in lung tuberculosis. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, Hft. 5.

The author makes detailed statements as to the methods of examination, emphasizing especially the possibility of erroneous results in examination of the pulmonary apex and hilus. He very properly states that the modern examination of the lungs included a roentgen examination, but that the roentgen method involves certain sources of error, against which it is necessary to guard. It goes without saying that the roentgen examination can never substitute, but only supplement, the clinical examination.

MARSCH, ERICH. Coincidence of tuberculosis and sarcoma. *Zentralbl. f. Chir.*, July 22, 1922, p. 1057.

Whereas the simultaneous appearance of tuberculosis and carcinoma has been repeatedly observed, the coincidence of tuberculosis and sarcoma has not, to the author's knowledge, been reported in the literature. Two such cases recently came under his observation, concerning boys, twelve and seventeen years of age respectively. The two cases corresponded in that after five and seven years, respectively, subsequent to the onset of bone and joint tuberculosis, an osteosarcoma and an enchondroma developed as sequelae of the healing tuberculous affection. Both of these patients had been treated for several years with roentgen rays. In the first case, an old tuberculous focus could still be demonstrated, while in the second case, although tubercles were no longer demonstrable, the diagnosis of fungus was undoubted. A purely accidental coincidence cannot be accepted as probable, but judging from the active course, the tuberculosis may be assumed to have acted as a predisposing factor, thus creating a place of lessened resistance for the development of the malignant neoplasm. In the absence of reasons for this unusual simultaneous appearance of the two diseases, the preliminary treatment with roentgen rays must be taken into consideration as an etiological factor for the sarcoma. It is possible that the malignant neoplasm developed as a result of the very frequent radiations to which the tuberculous knee-joints of these two patients were exposed; a sarcoma developing instead of a carcinoma, in conformity with their youthful age.

MEYER, P. S. Effect of *x*-rays on bacillus prodigiosis. *Klin.-therap. Wchnschr.*, Feb. 12, 1923, p. 297.

Summary: (1) A culture of Bacillus prodigiosus, after having once been treated with *x*-rays and damaged in its growth, will grow again in an entirely normal manner, but on repeated radiation, is less seriously damaged than culture which has not been previously radiated. (2) On continued radiation of this prodigiosus strain, the resistance becomes progressively more pronounced; it subsides when the strain is allowed to grow for four weeks without radiation, but at once reappears with the second repeated radiation. (3) This resistance corresponds to the immunity of bacteria against medicinal agents, and like this, may be interpreted as a transformation (Reichenbach). (4) The resistance is specific towards *x*-rays in that it does not exist towards ultraviolet rays.

HOFMANN, ARTUR HEINRICH. Compression of the stomach from high-lying colon. *Münchn. med. Wchnschr.*, Feb. 2, 1923, p. 149.

This observation concerned a man of thirty years, who, in getting down from a farm wagon, caught his foot and fell on his hands, head downwards. He had to remain a few minutes in this inverted position before he could free himself. Two hours later, severe abdominal pain supervened, and after a few days, he was admitted to the hospital under the diagnosis of gastric ulcer. The patient (who had always been well before the accident) could take only fluid food, everything else being vomited. Examination showed a bulging gastric fossa; the pyloric region was very tender to pressure. The roentgenogram showed a stomach looking as if cut off at the pyloric antrum. The paste was slightly less opaque in the middle of the lesser curvature, and a slight bulging was also somewhat suggestive of ulcer. The picture was the same at the end of six hours. At the operation, the transverse colon was found to be displaced upwards, and the ligamentum teres was tensely stretched, forming a prominent tendon which constricted the transverse colon and stomach. The stomach was voluminous, and no gastric ulcer was demonstrable. The abdominal coverings were closed after the colon had been replaced in its normal position, and the patient was discharged cured three weeks later. The case was one of displaced transverse colon, which in its turn had caused a compression of the stomach and was itself compressed by the ligamentum teres.

LAROCHE, G., BRODIN, P., and RONNEAUX, G. Critical study of chronic appendicitis: Importance of *x*-ray examination. *Presse méd.*, Apr. 8, 1922, p. 28.

The many types of chronic appendicitis make an exact diagnosis difficult. General symptoms and functional disturbances are not sufficiently characteristic to form the basis of a diagnosis. Defensive abdominal tension and the existence of a point constantly sensitive to pressure are of more definite significance; but the latter is difficult to demonstrate, because the location of the appendix is not always the same in different individuals. Of greater importance are the roentgenological findings; repeated examinations made with the patient in different positions will show a point sensitive to pressure at or very near the base of the appendix, that shifts in position with the appendix. For the examination, the cecum must be filled with contrast mixture (barium). Palpation is best carried out with the hand, which must, however, be protected from the prolonged radiation.

HOCHSTETTER. Duodenal stenosis following tuberculous peritonitis. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxix, Hft. 2.

A fifty-four-year-old man sent to the hospital with a diagnosis of gall-stones complained of attacks of colicky pains in the abdomen, especially at night, also of pains above the umbilicus after taking food, which were more severe when he was lying down than when sitting, also eructations, diarrhea and vomiting.

The roentgen examination showed the stomach drawn to the right, lying obliquely; no peristalsis, the stomach remaining filled and sausage-shaped after several hours. Foul-smelling contents were withdrawn by gastric lavage; operation showed an extreme stenosis of the ileum caused by a narrow cord-like band of connective tissue; also adhesions to the peritoneum. The patient died soon after operation.

OPITZ, ERICH. The problem of roentgen and radium dosage. *Klin.-therap. Wchnschr.*, Feb. 5, 1923, p. 243.

The author emphasizes, on the basis of a number of facts, that there exists no *x*-ray dosage through which carcinomatous tissue can be destroyed in every case, and this remark applies with even greater force to the so-called sarcoma dosage. The greatest difficulty for accurate dosage is referable to the general action of the rays. A part of the action of the rays is due not to a direct damage of the cancer cells, but to the general reaction of the body. The measuring of the *x*-ray doses is not only an arithmetical problem which has to discover the time plus the intensity of application. When the radiation, acting in a unit of time, drops below a certain low value (as easily occurs in actual practice) all possibility of success ceases, no matter how long the radiation be continued. Other difficulties arise in estimating the dosage of radium rays, and here again, the essential point is not merely the dose applied to a given carcinoma, but the amount of radium rays absorbed by the body as a whole. Aside from the quantity of radium or mesothorium employed, the position of the preparation and the absorption in the filter are of importance. In these chiefly gynecological applications the entire alpha radiation, and by far the greater part of the beta radiation are destroyed by the filters and thus do not exert an action in the body. It is of great significance for the general action, which portion of the gamma radiation comes to act upon the body, and this depends not only upon the filter material but also upon the thickness of the filter.

PAUCHET, VICTOR. Diverticula of the colon. *Gaz. d. hôp.*, 1922, xcv, No. 41.

Diverticula of the colon are hernia of the mucosa, often resulting from constipation; they are well demonstrated by the roentgen ray after bismuth enema. They are often filled with feces and may cause pelvic abscesses, peritonitis, contractions or inflammatory tumors. So long as there are no symptoms due to the diverticula, it is sufficient to treat the constipation. Abscess formation is an indication for drainage; fistulae for resection of the portion of the intestine involved. Inflammatory tumors must be treated like carcinoma, with the difference that the artificial anus need not be made permanent.

FEISSLY and FRIED. Etiology of the "cascade stomach." *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxix, Hft. 2.

Description of a case with operation. The operative findings were as follows: The omentum majus was adherent to the anterior abdominal wall; this was detached. The stomach was free, showing no constriction, no sac formation, no scar, neither active nor latent ulcer, no tumor. The posterior gastric wall was far removed from the colon. Pylorus patent, no duodenal ulcer. Pancreas and perigastric region normal. The liver extended slightly above the costal arch. The gall-bladder was small; no concretions in the biliary passages. The gall-bladder was enclosed in a tough membrane full of small blood-vessels; this membrane was detached. A short mesocolon and a very short ligamentum hepatogastricum were found. It is possible that the biloc-

ular shape of the stomach was due to the shortness of this ligament, and also to the adhesions around the gall-bladder. Closure of the wound, which healed normally. Later the patient showed the same symptoms as previous to operation. At the second operation, the findings were as follows: The epiploon was closely adherent to the anterior abdominal wall, the liver and surrounding organs. The colon with the ligamentum gastrocolicum was drawn upwards and the stomach therefore held in an abnormally high position by this ligament. The pars pylorica of the stomach was indented by the abnormal insertion of the ligament. The adhesions were freed with difficulty. The stomach showed nothing abnormal; spleen and kidneys normal. The operation consisted in freeing adhesions and releasing the colon and the liver.

A month after the operation, the roentgen examination again showed the typical cascade stomach. It appears that the cascade stomach was caused by the pull of the transverse colon. The short ligamentum hepatogastricum found at operation may have drawn the stomach too far upwards while the short mesocolon and the pressure of the transverse colon cooperated in producing the result. And since the patient had very probably suffered from some inflammatory condition previously, this was also a factor in the high fixation of the colon. After the operation, the extensive adhesions reformed, which caused an accentuation of the cascade form, and the development of a true cascade stomach.

In classifying the various types of this form of stomach, distinction should be made, first, between the true and the false cascade stomach. The latter includes those types caused by spasm, air in the colon, which are variable and usually respond to treatment with belladonna and atropin, as Carman has described. The true cascade stomach is characterized by the permanence of its form, and can be caused by (*a*) pathological conditions in the stomach (ulcer, scars); (*b*) pathological conditions in the perigastric region (perigastritis, peritonitis, extraventricular tumors); (*c*) changes in the normal course of the colon.

Naturally in certain individual cases spasm may be caused by an ulcer.

KAREWSKI, F. Intussusception of the descending colon. *Deutsche. med. Wchnschr.*, 1921, No. 34, p. 990.

A case report of an intussusception of the large intestine, 25 cm. long, caused by an adenomatous carcinoma of the intestinal wall, of the size of a mandarin, and with a wide base. On the basis of the roentgenological appearance, the author came to the conclusion that an unusually low location of the flexura linealis, most probably due to a general invagination of the descending colon, together with a palpable mobile tumor, indicated a still patent invagination.

ZEHBE. Duodenojejunal diverticula. I. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 2.

The five diagnostic criteria of duodenojejunal diverticulum described by Forsell were all fulfilled in the case reported by Zehbe in a thirty-five-year-old man. For two years there were indefinite pains in the upper and middle abdomen, radiating sometimes toward the liver, sometimes toward the sacral region, often disturbing the night's sleep. These attacks of pain lasted for weeks and months and then would entirely disappear for a time; no vomiting, no heartburn, occasional constipation. Alexander Adams operation without result. Roentgenogram of the stomach showed nothing unusual. The canalis egestorius showed a somewhat rapid peristalsis, which caused the rapid passage of the gastric contents into the duodenum through the pylorus, which was almost constantly open. The duodenal bulb was small, contracted rapidly and strongly, and discharged its contents into a space the size of a goose-egg, which filled rapidly and was situated with its lower pole between the duodenal bulb, the pars pylorica and the stomach. This space, as demonstrated by repeated roentgenological examination, was divided into several sections by folds in the wall and lay eccentric to the duodenum. Its lower pole retained the contrast meal, its upper pole an air vesicle; between these was an intermediary layer. No definite diagnosis was made. Operation showed normal stomach with a few adhesions at the pylorus. Palpation of the duodenum did not give the slightest indication of a diverticulum. The operation did not relieve the symptoms and the roentgen-ray findings were the same after operation as before.

KOHL, F. New treatment lamps for constitutional heliotherapy. *Strahlentherapie*, xii, 994.

Description of two new types of lamps: "Efka" lamp and "Efkaheliol" lamp. The former is a carbon arc lamp with an open burner, in which so-called "effect carbon" is utilized for the production of light, as rich as possible in ultraviolet rays. Four successive light arcs are provided for, and the author adds that the lamps are equipped with an appliance for the removal of injurious vapors. The "heliol" lamp is based upon an altogether different principle; it is a carbon light arc enclosed in a space poor in oxygen. With this

adjustment, it is possible to increase the tension. The carbon consumption is much less considerable. Instead of carbon dioxide, only carbon oxide is formed, which provides a better conductivity for the electric current. By means of this increased tension, a light very rich in ultraviolet rays is obtained. By selecting quartz or different kinds of glass for the enclosure of the source of light, it is possible to keep in stock burners with an entirely different spectrum, for different purposes. The lamp can be ordered from Fritz Kohl, *55* Bruderstr., Leipzic.

EISLER. A rare case of Paget's disease. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxix, No. 3.

Multiple joint affections are not infrequently observed in syphilis; the affection of a single joint may likewise occur, and often remains unrecognized as such. Surgical interventions in these misinterpreted cases are injurious. Monoarticular joint disease may be due to congenital as well as acquired syphilis; in the secondary stage, its recognition is not difficult in acquired syphilis, whereas the diagnosis is extremely difficult in the tertiary stage, where in the absence of other syphilitic manifestations, confusions may occur with sporotrichosis, sarcoma, and especially with tuberculosis. The chief differential features with respect to tuberculosis may be summarized as follows: In tuberculosis, weakness of the body, pain on movement, fistulas, cutaneous venous plexus, enlarged glands; relief through rest and fixation. In syphilis, slight tenderness, a strong body, no fistulas, no relief through fixation; a positive Wassermann reaction, and curative effect of antisyphilitic treatment. In monoarticular arthritis, the process may originate from the cartilage as well as from the joint capsule. Eleven cases, observed by the author, are described; 4 of these cases concerned the shoulder joint, 2 the elbow joint, 1 the wrist, 3 the knee and 1 the ankle joint. As shown by accompanying roentgenograms the articular ends were eroded in many cases.

SAUER, H. Osteitis fibrosa. *Deutsche. Ztschr. f. Chir.*, Apr., 1922, clii, 95.

Only those cases of generalized fibrous osteitis which have been investigated clinically, roentgenologically and histologically, and which finally come to autopsy, can furnish information as to the pathogenesis of the disease. The author contributes such a case from the Ringel Department of the St. George Hospital in Hamburg. The patient finally died as a result of complications, after a course of seven years, with periodical arrests and aggravations. The disease appeared in a boy of sixteen years, free from all signs of rickets, as a result of a fall into ice-cold water. Observations during four years again showed that the apparently highly variegated pictures are merely varieties of the same pathological process and represent only stages in the constantly changing picture of the disease. The nature of the process consists in a complete transformation of the bone tissue and substitution of the bone marrow by fibrous tissue in part, with productions of tumor-like structures, which histologically appear either as pure fibromas or as giant-cell sarcomas. Smooth-walled cysts surrounded by solid spongy tissue are the terminal stage of the entire disease, representing a sort of cure. The course of Sauer's case showed a remarkable improvement in the upper limbs, whereas the condition of the lower limbs had rather become aggravated. The fatal outcome was due to a complication in the form of angular kinking of the vertebral column at the transition of the thoracic segment with the lumbar segment, with pressure upon the spinal cord.

The autopsy showed a tumor of the left inferior parathyroid gland, which is referred to by the author as responsible for the pathogenesis of the osteitis fibrosa. Brief clinical histories are given of 11 cases of localized osteitis fibrosa, part of the tumor-forming type, part manifesting themselves as bone cysts. Localization in the ischium was observed in two instances. The prognosis of the localized tumor-forming type is relatively favorable. In the course of years, a sort of spontaneous cure is possible without any therapeutic intervention. The healing process can be accelerated through exposure of the bone focus. This intervention is at first followed by an enlargement of the focus, as after a fracture of diseased bone. The giant cell containing tissue is gradually replaced by newly developed spongy tissue. The bone cysts were all observed on the occasion of a spontaneous fracture. In view of the fact that cases which have not been operated upon have a greater tendency to repeated fractures than the excochleated cases, the treatment should always consist in operative exposure and scraping the cavity. Eleven of the twelve cases concerned the female sex. The age varied between nine and fourteen years.

BAENSCH AND BOEMINGHAUS. *X*-ray differentiation of diseases of the uropoietic system. *Ztschr. f. urol. Chir.*, 1921, vii.

The writer discusses fully the roentgen diagnosis of the uropoietic system and describes the methods used at the Voelcker Clinic. Every roentgenological examination of the kidneys is begun with a bilateral plate (compression dia-

phragm) in order to avoid errors from contrast materials that persist in situ. Inflation of the abdomen with gas is much used; Goetz technique; introduction of needle through the rectus muscle, insufflation of oxygen. Weak tubes. Before the screen the patient is turned slowly from the dorsal position to the right side, thus lifting the left kidney slowly about 40° out of the deep shadow complex of the back musculature, spinal column and intestines. On the right side conditions are more unfavorable, as here the liver covers the upper pole of the kidney almost completely. Good plates are obtained with the patient in the dorsal position. After the examination, the oxygen is with drawn through a trocar. Serious reactions were never observed. The pyelogram is a valuable aid in roentgenological diagnosis. Only moderately large ureteral catheters should be used so that the collargol can flow back into the bladder on both sides. Injection must be made slowly. The renal pelvis should first be emptied of all residual urine, as otherwise the plates may not be clear owing to great dilution of the collargol. Very clear plates may also be made by the simultaneous inflation of the ureter and the abdominal cavity with air. This method has given excellent results in diagnosis. Unilateral kidney aplasia, horseshoe kidney, and floating kidney can be definitely diagnosed. From the plates conclusions can be drawn as to the isolated and combined enlargement of individual parts of the kidney pelvis and calyx. Mechanical obstructions to urinary flow cause primary dilatation of the so-called anatomical kidney pelvis, while with primary infection, the pelvis at first remains intact, and the capacity of the fornices enlarged partly through dilation, partly through suppurative fusion. Primary dilatation can also be combined with infection (acute and chronic dilatation pyonephrosis). In acute cases ureteral catheterization is contraindicated, as injury to the mucous membrane from the catheter may result in contamination of the blood stream. Kidney tuberculosis is a difficult field, as the process is usually far advanced before it presents a definite roentgenogram. The pathological changes affect chiefly the fornices and calices of the second order. Pneumoperitoneum and air inflation are especially valuable in the diagnosis of kidney stones and of tumor. The ureter is clearly shown in the roentgenological picture; the ureteral catheter can be introduced into the ureteral orifice a few centimeters and then contrast material allowed to flow in. If a contrast catheter is used this stretches the ureter, and pathological kinks are not visible. In insufficiency of the ureteral orifice, excellent plates are obtained if the bladder is filled with collargol, and the patient asked to attempt to urinate, but holding the urethra together. Further, the changes in the bladder during normal micturition, prolapse, pregnancy, hernia, diverticula and hypertrophied prostate are described; also the roentgenological technique for the diagnosis of bladder calculi. The radiological study of the prostate is of only slight value, and methods of making roentgenograms of the seminal vesicles have not been made clinically useful. The same is true of the urethra.

HENSZELMANN. The diagnostic value of colon inflation in the diagnosis of spleen, liver and gall-bladder disease. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxix, No. 4.

The author describes the technique for inflation of the colon with an ordinary type of bellows; this was done at first with the patient upright; later, lying on the left side, as in this latter position the inflation is more uniform and the procedure is better borne. Two hundred to 400 c.c. of air should be introduced four to five times. The intestines should be emptied previously. The outlines of the liver and spleen are very clearly demonstrated; also the pancreas becomes visible. The air can be introduced while the intestine is filled with contrast material. The author presents several illustrations showing his results, for example, a gall-bladder filled with stones, tumors of the spleen and liver, etc.

VOGT. Gastrointestinal examination of the newborn. *Fortsch. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 4.

"Citobarium" is not injurious even for newborn infants who do not refuse to take it. The dose is from 20 to 30 gm. in a thin fluid drinkable infusion. For an enema, a mixture of 20 to 40 gms. with water is used. The usual shape is the angle-hook form, more nearly syphone form. The gastric air bubble is largest immediately after the meal. The stomach is divided into the cardiac portion, the fundus and the pyloric portion. The empty stomach is tubular. The body axis and the stomach axis form an acute angle with each other. The medium time of evacuation of the stomach amounts to one and a half to three hours with mother's milk, somewhat longer with cow's milk. The ileum opens rectangularly into the cecum. The last coil of the ileum descends only as far as the pelvis. The small intestine has the most marked peristalsis. In three hours, the ingested material has passed through the small intestine. The transverse colon takes a gibbet-shaped, extended course. The coil of the descending colon is characterized by great fluctuations with respect to its extent, arrangement and position. The con-

trast mixture remains three to four hours in the large bowel, after which time it is gradually evacuated. The digestion of a meal consisting of mother's milk requires, on an average, from five to eight hours.

CATTANEO. Subacute and chronic monoarthritis as the only manifestation of luetic infection. *Radiologica med.*, ix, No. 4.

Description of a case. The summary follows. Our case is of interest for several reasons: (1) Paget's bone disease, which is known to cause no clinical or subjective symptoms of any kind at the beginning, can first be recognized in the roentgenogram, principally in a diffuse calcium deficiency of the bone; it is not until later on that hypertrophic changes and deformities make their appearance, as a transformation of the bone tissue of characteristic type. (2) A fracture may complete the decalcification of the bone. (3) Although the calcium deficiency is gradually replaced, the typical deformity producing change of the bone now sets in. (4) Furthermore, the case serves to show that fractures of atypical site and appearance should always direct attention to a pathological condition of the bony framework.

WOLFF, E. Diagnosis of high lesser curvature ulcers. *Klin.-therap. Wchnschr.*, 1922, No. 3.

The author shows with many illustrations how an ulcer below the cardia on the lesser curvature of the stomach may often be demonstrated if the patient lies on the left side. Excellent roentgenograms add to the text.

SCHINZ, H. R. The roentgen appearance of stomach ulcers. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, xxxiv (supplement).

This excellent report deals with the peptic ulcer cases studied at the Central Roentgen Institute of the cantonal hospitals of Zurich in the last two years (66 cases) and is of special value because the author was present at each operation and could compare the operative with the roentgenological findings. The many resections done by Professor Claimont yielded especially interesting results in duodenal ulcer. The number of ulcers that were correctly diagnosed and localized is astonishingly large; on the basis of his report, the author concludes rightly that every ulcus callosum can be recognized by the roentgenogram. The cases are described in detail under the following classification: 1. Ulcera callosa of the pars cardiaca of the stomach. 2. Ulcera callosa of the pars media of the stomach (*a*) on or near the lesser curvature, (*b*) on lateral surfaces, (*c*) on the greater curvature. 3. Ulcera callosa of the pars prepylorica. 4. Duodenal ulcers. 5. Mucous membrane ulcers.

The author's statements in regard to the clinical picture and the position of the ulcer are especially valuable. He shows that the clinical picture depends upon a variety of constitutional factors and other conditions, but gives no definite evidence for the localization of the ulcer. Late pains may occur in ulcers at a distance from the pylorus. The only means of localizing ulcers is the roentgenological examination, and in the hands of an experienced roentgenologist, it is a sure means. In addition to localizing the site of the ulcer, the roentgen examination also gives information in regard to the nature of the ulcer, and in this way indicates the necessary treatment, in that all stenosing and penetrating ulcers are absolute indications for operation. A definite diagnosis of mucous membrane ulcers is not possible. The value of the roentgenological examination is in demonstrating the presence of an ulcus callosum, since such cases are suitable for medical treatment.

The treatise is very valuable. It gives a number of important suggestions and urges each roentgenologist to develop his own technique for examinations. The work can be recommended to every surgeon.

HACKRADT. The position of the patient in relation to treatment with natural sunshine. *Strahlentherapie*, xii, 1015.

Upon the basis of numerous measurements as well as mathematical deductions, the author arrives at the following conclusions: The radiation should be applied in the recumbent position, in order to guard against increased congestion of the lower extremity. From a distance of 40 cm., the intensity of the quartz lamp light diminished in about the square of the distance. For radiation of the entire body with artificial sunlight, a distance equal to half the length of the body should be selected. The body axis and the light tube axis should go parallel. For entire radiations, the work is most economically done with two lamps, having a distance of 70 cm. from each other, and a distance of 50 cm. from the patient. The consumption of electric current is hardly greater than when only one lamp is used.

GROEDEL, FRANZ M. Roentgen symptomatology of duodenal ulcer. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, xxxiv, No. 2.

The roentgenological side of the diagnosis of ulcus duodeni is discussed in a brief but illuminating way in this article, which can be recommended to the attention of every surgeon and every physician studying roentgenology. In general, the author states that the roentgenogram of the diseases to be differentiated are remarkably similar. This is probably due to the fact that they all have the same genetic

basis, depending upon abnormal function of the vegetative nervous system. On the other hand, the special roentgenogram of ulcus duodeni is sufficiently characteristic, that as a rule the diagnosis can be correctly made with due consideration of the clinical symptoms.

DALIMIER. Pseudo-cancer of the stomach of syphilitic origin. *Gaz. d. hôp.*, 1922, xcv, No. 2.

This article reports a case of syphilis of the stomach which clinically and roentgenologically simulated carcinoma, with cachexia, which was cured in four weeks by specific treatment.

HROMADA, G. Insufficiency of the ileocecal valve. *Arch. f. klin. Chir.*, 1921, xcvii, 784.

Embryological studies and animal experiments show that normally the valvula Bauhini can be closed. The valve is actively closed by contraction of the m. sphincter ileocolicus both toward the ileum and toward the cecum, and passively serves as a valve against regurgitation from the large intestine. In cases of insufficiency of the valve due to adhesions, etc., a corrective operation by the simple technique of Kellogg or Payr relieves this insufficiency. The method of Kellogg consists in infolding the ileum in the colon. Payr suggested that by means of a simple Lembert suture between the cecum and the upper wall of the ileum, the ileum could be lifted and the normal ileocecal curve reestablished, which guarantees the sufficiency of the valve. This operation has been done in the Leipsic Clinic 16 times; twice the insufficiency of the valve was due to enlarged mesenteric glands; in 6 cases to adhesions after previous operations, and in 9, to adhesions after appendicitis. The symptoms of the patients were all the same, chiefly chronic constipation on which the usual methods of treatment had no effect. After relieving the insufficiency of the valve these symptoms were remarkably improved.

BÉCLÈRE, A. *X*-ray treatment of intra-abdominal manifestations of malignant disease of the testicle. *Strahlentherapie*, xii, 1058.

The patient was a man of thirty-five years in whose case a tumor developed as a sequel of retained testicle, and was removed two years ago by operation. The present condition was one of advanced cachexia with an enormous intra-abdominal tumor. Multiple-fields radiation; filter 1 mm. aluminum; one weekly treatment during several months. Complete subsidence of the tumor, and cure persisting five years at the time of the report. One year after the radiation a small *x*-ray ulcer appeared and was checked through transplantation. The histological examination of the tumor, which was found at the first operation, showed a seminal epithelioma, a so-called seminoma, which in conformity with its origin, was enormously sensitive to the action of the *x*-rays.

ZEHBE. Duodenojejunal diverticula. II. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxvii, No. 5.

A somewhat atypical symptom complex with periodical attacks, gastric pain persisting several hours after meals and at night, radiation of the pain from the mid-line to both sides and also to the back, with nausea, eructations, and sometimes vomiting without hematemesis, suggesting duodenal ulcer, could not be correctly diagnosed, but roentgen examinations during the last three years have shown that these symptoms were due to diverticula in the upper intestine. Three types of diverticula are distinguished according to their location: (1) On the pars media of the duodenum near Vater's papilla; roentgenologically these diverticula are shown below the bulbus duodeni; (2) in the terminal portion of the duodenum (pars ascendens d. ramus inferior)—the shadow of such a diverticulum lies medial to the lesser curvature of the stomach, somewhere between the bulbus duodeni and the angulus ventriculi; (3) in the upper loop of the jejunum below the duodenojejunal flexure. The shadow of a diverticulum of this type is seen in the region of the upper half of the stomach, lateral to the lesser curvature. The correct localization of such diverticula is of clinical as well as scientific interest. While the surgical removal of a diverticulum on the pars media is perfectly possible, a diverticulum located on the upper part of the jejunum, i.e., near the flexure, would be extremely difficult. With the low duodenal diverticula, just above the flexure, lying retroperitoneally, operation is contraindicated according to present knowledge.

VOGT, E. Combination of operative and roentgen therapy for genital tuberculosis. *Deutsche med. Wchnschr.*, 1921, No. 11.

The purely conservative treatment of genital tuberculosis in the female is suitable only in very mild cases, or in cases in which neither operation nor roentgen-ray treatment can be employed for some reason. The great advantage of operative treatment is that only in this way can definite knowledge be obtained in regard to the severity and extent of the disease. However, operative treatment has certain disadvantages. In order to prevent recurrences, operation should be followed by prophylactic roentgen-ray treatment. If operation is impossible for any reason, the roentgen-ray treatment alone may be used with good results, and without danger.

SIEGEL, P. W. Life expectancy of the uterine cancer patient. *Strahlentherapie*, xii, 97.

Following up König's studies, the author presents the results in uterine carcinoma at the Giessen Gynecological Clinic for 1905 to 1915. On the whole, his results correspond fairly well with König's. While König found the average duration of life in inoperable cases of cervix carcinoma to be one and three-fourths years, and in the operated cases one and one-half years, Siegel found the average duration of life in inoperable cases of this type to be two and one-fourth years, and in the operated cases two and three-fourths years. Operation, therefore, in his cases prolonged life half a year on the average. Five years after the beginning of treatment, 24 per cent of the patients operated for cervix cancer and 13 per cent of those with inoperable carcinoma were living. The results in operated cases were somewhat better in cancer of the corpus uteri. The author believes that roentgen-ray treatment of operable uterine carcinoma in large, properly equipped, special institutions is well justified. He advises fewer radical operations in order to reduce the primary mortality, and the substitution of less extensive operative procedures for removal of the growth, followed by intensive roentgen-ray treatment.

SMIDT, HANS. Roentgenologic study of the condition of the stomach during gall-stone colic. *Arch. f. klin. Chir.*, 1921, xcvii, 425.

Eight cases of gall-stone were studied roentgenologically in regard to gastric function during an attack. During an acute attack there is a definitely increased tonus of the entire gastric wall. This hypertonia is accompanied by the development of a spastic condition. The excessive irritation connected with an attack of gall-bladder disease is communicated reflexly to the gastrointestinal tract, and produces the irritative condition described. As the attack ceases, the stomach shows evidence of exhaustion. The gastric symptom complex observed during and after acute attacks of biliary colic is to be considered as a reflex neurosis.

DEHN. A hypophyseal tumor: case report. *Fortschr. a. d. Geb. d. Röentgenstrahlen*, xxix, No. 5.

Patient, a male, thirty-five years (descended from healthy parents) presented the appearance of a small child. The *x*-ray examination showed the following findings: All the epiphyseal lines were preserved, the bones of the head resembling those of a child of ten years; but the phalanges and metacarpals were remarkably thick and short. Both hip-joints presented an advanced coxa vara; the femoral neck formed an acute angle with the shaft, the trochanter major was in contact with the anterior superior iliac spine. The epiphyseal lines were preserved also in this locality; the knee-joint was likewise distinctly deformed; the bones (femur, tibia and fibula) showed an unusual loose-meshed bone structure; likewise the bones of the foot. The skull, aside from the well-marked sutures, presented a distinct diminution in the size of the sella turcica, the dorsum of the sella being thickened in such a way as to produce the impression of a solid square bone instead of a bone plate. The posterior and anterior clinoid processes were approximated to each other in such a way as to be nearly in contact. The bones of the facial skull were relatively undeveloped as compared to the brain capsule. The behavior of the sella turcica, as well as the entire condition of the patient, were in striking contrast with acromegaly. This is in entire conformity with the rule: atrophy of the hypophysis in infantilism; hypertrophy of the hypophysis in acromegaly. The patient subsequently died of pneumonia. At the autopsy, the hypophysis was found to be of normal size, but in a state of cystic degeneration, with gelatinous contents. The dorsum sellae was found to be cartilaginous without traces of ossification, so that it could be cut with scissors.

LESI. Echinococcus cyst of the tibia. *Arch. ital. di chir.*, Oct., 1921.

Echinococcus cysts in bones are very rare, and according to Lejars (1907) about 82 cases had been reported up to 1907. The echinococcus parasite acts in the bone through pressure and through ischemia, resulting in evacuation and necrosis. The echinococcus embryo passes from the intestine through the portal vein and the venous circulation into the right heart, and from here through the lungs into the left heart, whence it is carried to the peripheral arteries of the bones. Traumatism of the bones may favor the lodging of the parasite or may stimulate a quiescent echinococcus cyst in the bone to an increased size and extent. The symptoms consist of mild bone pains, swelling of the bones and spontaneous fractures. As a rule, multilocular cysts are present. From the viewpoint of the differential diagnosis, bone sarcoma and bone tuberculosis enter into consideration. The author reports an illustrative case which came under his observation. The patient, a girl of twenty-five years, suffered a contusion of the left knee by a fall; walking was not impaired later on, but there was persistent slight painfulness, followed some months later by swelling in the region of the knee. A fluctuating locality was incised, with evacuation of a yellowish fluid. No improve-

ment followed and the patient was admitted to the hospital, where a large cavity in the upper tibial epiphysis was demonstrated by roentgenogram. Surgical intervention with removal of numerous echinococcus cysts was followed by a very protracted recovery, with intermittent fever.

GALEWSKY, E. Roentgen dermatitis vs. salvarsan dermatitis. *Dermat. Wchnschr.*, 1921, No. 31.

The author reports a case in which a circumscribed dermatitis developed after a roentgen-ray examination in the exact area affected by the rays, and following this a salvarsan dermatitis appeared.

STARK. Progress in deep roentgen therapy. *Strahlentherapie*, xii, 1024.

Report of cases treated during the last year. A very large material from all domains was irradiated (surgical tuberculosis, goiters, skin diseases, tumors, gynecological cases). In a general way, good results were obtained in tuberculosis of variable localization. The demand which has been made to administer 100 per cent of the skin unit dose to a tuberculous joint must not be left unchallenged. After such large doses, extremely grave remote lesions may appear in the extremities (chronic indurated cutaneous edema, scar formation, contractures, circulatory disturbances, ulcers). It is true that these remote lesions are not observed in the first year, but eventually only, at the end of one year after the last irradiation. The writer of the abstract in the *Zentralblatt für Chirurgie* (1922, No. 32, p. 1205) urgently cautions against such high doses, on the basis of several years' experience. The author believes, however, that remote *x*-ray lesions which appear later than about six months after the radiation have no real existence as direct sequelae of the radiation; but he admits that there exists a grave alteration of the tissues, produced through the rays, which renders the tissues hypersensitive to mechanical, bacterial and other stimuli. The tissues must be protected against all injuries. The author assumes that the danger is probably past at the end of a year or two, but his experience is too short for the decision of this question. In the opinion of the abstract writer, the report of such brief observations is of no particular value for surgical *x*-ray therapy. In malignant tumors, the permanent results are of essential interest, and in bone and joint tuberculosis, with its protracted process, an observation of cases treated last year hardly permits a verdict as to the value of the method of treatment.

HERRNHEISER. Pseudo-diverticulum of the duodenum. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, xxviii, No. 4.

Description of a case. The patient was a glassblower, forty-eight years of age, who, for thirteen weeks, had suffered from severe gastric disturbances. A resistance, painful on pressure, was found two fingers' width below the costal arch. The roentgenogram showed at the boundary of the upper and lower third of the descending duodenal segment, a mesially situated, rounded, sharply outlined diverticular evagination, about the size of a hazelnut, and extremely tender on pressure. The autopsy showed a secondary carcinoma of the entire pancreas, in the corpus and cauda (tail) in the form of still indistinct nodules, in the caput (head) in the form of diffuse infiltration, extending to the descending portion of the duodenum, with a duodenal diverticulum, the size of a walnut. Secondary carcinoma of both suprarenals, with almost complete destruction of these organs. Histological examination of the diverticular evagination of the duodenum showed the condition to be due to invasion of the tumor into the duodenal wall, evidently with grafting of a peptic ulcer on the tumor. According to the histological findings, the tumor corresponded to bronchial carcinoma and represented a small cellular infiltrating carcinoma.

Summary: (1) A pancreatic carcinoma, with involvement of the duodenum, without production of stenosis, may form a smooth-walled disintegration cavity, as the result of peptic ulceration, so as to simulate closely the picture of a diverticulum in the roentgenogram. (2) As compared to a carcinomatous pseudodiverticulum of this kind, the demonstration of extensive mobility, and especially a positive Freud symptom, would be decisive in the differential diagnosis. (3) In case of a negative outcome of the symptoms mentioned under (2), all clinical methods should be utilized for a decision in suspected cases, with special differentiation of the organs which enter into consideration as the starting point for pancreatic metastases.

KURTZAHN, H. Roentgen dosage and roentgen burns. *Deutsche. med. Wchnschr.*, 1921, No. 44, p. 1326.

Upon the basis of personal experience, the author objects to the statements made by Liek (*Deutsche med. Wchnschr.*, 1921, No. 34, p. 999) and confronts these statements with the observations made in the Königsberg Surgical University Clinic, as well as with the principles of *x*-ray irradiation based on other findings.

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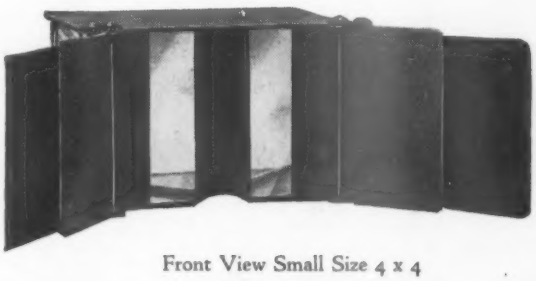

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PUBLISHED MONTHLY BY PAUL B. HOEBER, INC.
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IMPORTANT NOTICE

Subscribers will have noticed the increase in size of THE AMERICAN JOURNAL OF ROENTGENOLOGY & RADIUM THERAPY during the past few years. Vol. 1, 1914, contained 495 pages, Vol. IX, 1922, 856 pages, and the volume for 1923 will be even larger. Despite this the editors have had to exclude much splendid material in order to keep within bounds.

There is no necessity to explain the increase in costs since 1914 and we may point with pride to the fact that despite this increase, which ran parallel with the doubling in size of the Journal, the subscription price has been raised only $1.00, from $5.00 to $6.00. This was made possible only by the support given the Journal by The American Roentgen Ray Society.

Dr. Arthur C. Christie of Washington, D.C., is to be editor beginning January 1924. The plans for next year call for a Journal of at least 1200 pages, divided into two volumes, with an index in July as well as in December. While it is realized that the Journal is recognized today as the leading x-ray journal in the world, those in charge still feel that further improvements are possible and that our readers are entitled to the very best that can possibly be attained. Arrangements have been made for a complete abstract department, more illustrations, and further improvements in every department. The editorial policy will be a vigorous one and it is expected that THE AMERICAN JOURNAL OF ROENTGENOLOGY & RADIUM THERAPY will cover every branch of the subjects named in its title.

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VOL. X · DECEMBER, 1923 · NO. 12

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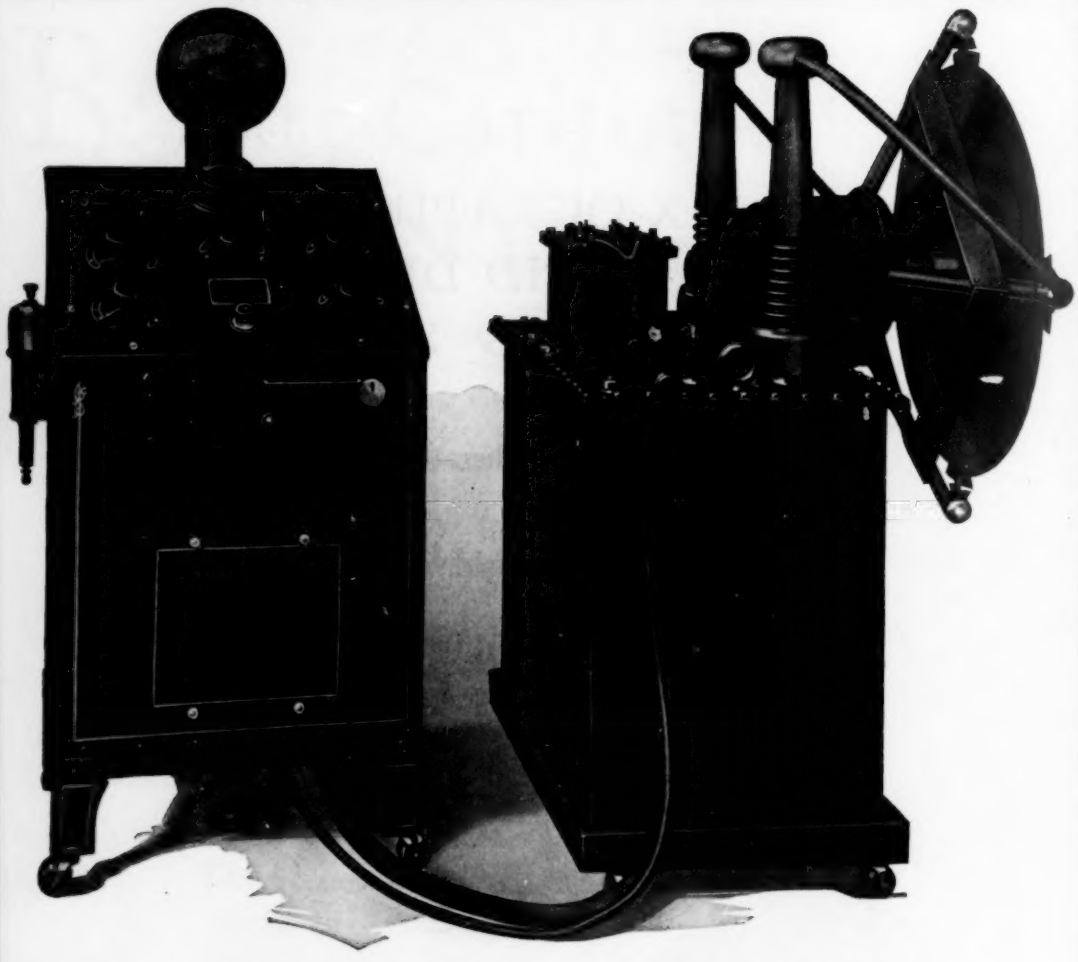

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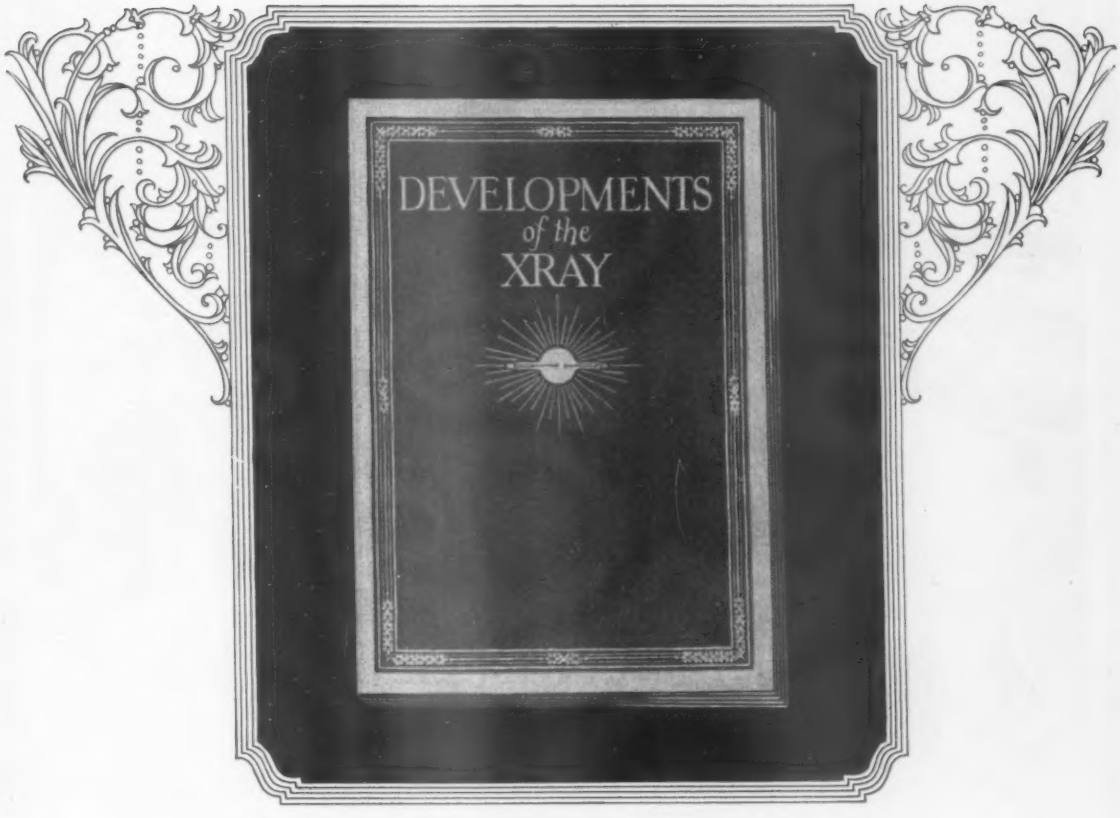

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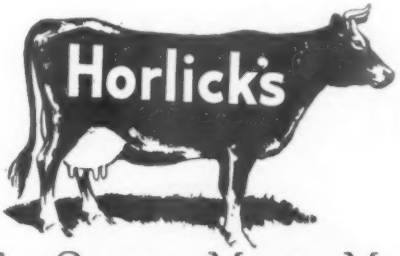

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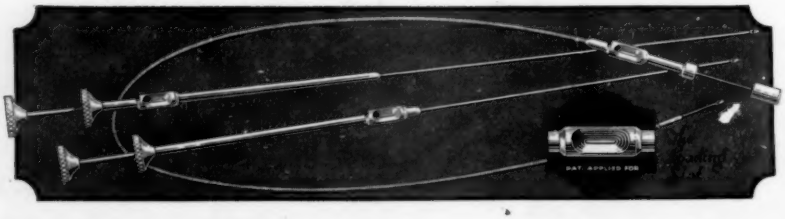

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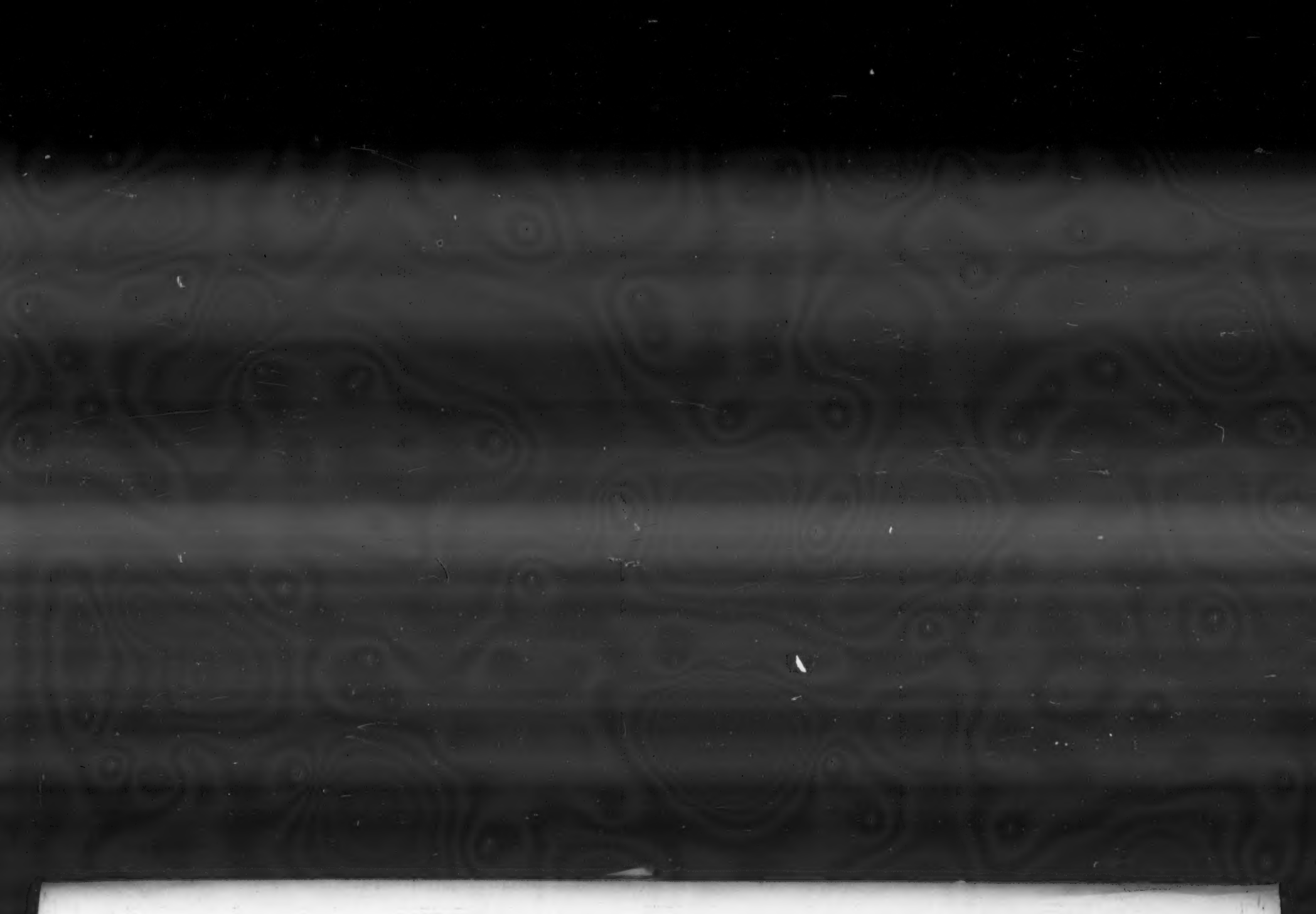
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